UNIVERSITY OF LONDON THESIS

Degree PhD Year 2007 Name of Author HOFFMAN, Kathryn Elizabeth

Reported pain in multiple sclerosis (MS) and its relationship with affect and attention

Kathryn Elizabeth Hoffman

Thesis submitted for the degree of Doctor of Philosophy
University of London

Department of Brain Repair and Rehabilitation
Institute of Neurology
University College London
Queen Square
London WC1N 3BG

August 2007

ProQuest LLC
789 East Eisenhower Parkway
P.O. Box 1346
Ann Arbor, MI 48106-1346

Declaration

I declare that the work presented in this thesis is the result of my own investigation.

Kathryn Elizabeth Hoffman

ACKNOWLEDGEMENTS

I would like to thank my advisors Dr. Dawn Langdon and Professor Alan Thompson for all their help and support. I would also like to thank the Multiple Sclerosis Trust for their funding of this project and the Central Research Fund, University of London for supplying funds toward project expenses.

TABLE OF CONTENTS

TABLE OF TABLES and FIGURES

ABSTRACT

Pain is an important part of MS symptomatology. Studies, with other pain populations, suggest distress is associated with pain. However, models of the influence of psychological factors on pain have not been carefully applied and tested with the MS population.

The hypothesis was: many patients do not classify much of their sensory disturbance as pain due to their conceptual framework and this may affect the relationship between pain and distress. A model of these factors was developed for MS patients.

A clinic sample of MS patients, expected to have varying degrees of subjective pain, was recruited. Standard, adapted and new measures were used to characterise the population along the following dimensions: pain, level of cognitive ability (general intelligence and working memory) and cognitive bias, mood, and coping styles. Amount of distress was assessed using a semantic differential measure of wellbeing/distress, Survey of Pain Attitudes and Coping with MS Scale. A Pain Discomfort Scale was adapted to discern differences between people reporting "pain" versus those reporting "discomfort." Pain cognitive-processing bias was explored using assessments including a stem completion task, an experimental recall task using pain and illness words and a restructured Hayling sentence completion task. Power calculations showed that with 100 patients a detectable correlation would be 0.28 ($p=0.05$, power = 80%). Measures were compared using paired t-tests for repeated measures, independent t-tests for measures across patients, and regression modelling.

McGill adjectives chosen were similar across both high and low pain responders. Participants reporting "pain" experienced significantly greater physical impact of MS whereas participants reporting "discomfort" experienced greater emotional distress. Cognitive bias towards pain, illness and MS related material was not linked with overall pain or disease state but with coping styles. A model of how emotional stressors affect reported pain in MS was created.

ACRONYM LIST

BADS = Behavioural Assessment of Dysexecutive Syndrome

BN = Benign

BI = Barthel Index

CBT = Cognitive Behavioural Therapy

CMDI = Chicago Multiscale Depression Inventory

CMSS = Coping with MS Scale

CNS = Central nervous system

CP = Chronic Progressive

CVLT = California Verbal Learning Task

EAE = Experimental Autoimmune Encephalomyelitis

EDSS = Expanded Disability Status Scale

ERLT = Experimental Recall Learning Task

FDS = Fatigue Descriptive Scale

FIM = Functional Independence Measure

fMRI = Functional Magnetic Resonance Imaging

FIS = Fatigue Impact Scale

FQS = Fatigue Questionnaire Scale

GHQ = General Health Questionnaire

HADS = Hospital Anxiety and Depression Scale

HAS = Hospital Anxiety Scale

HDS = Hospital Depression Scale

HQOL = Health Related Quality of Life

IASP = International Association for the Study of Pain

JAMA = Journal of the American Medical Association

KFSS = Krupp Fatigue Severity Scale

MCM = mood-congruent memory

MHI = Mental Health Inventory

MS = Multiple Sclerosis

MSIS = Multiple Sclerosis Impact Scale

MRI = Magnetic Resonance Imaging

NART = National Adult Reading Test

PD = Pain Discomfort Scale (adapted version)

PDS = Pain Discomfort Scale (original version)

PP = Primary Progressive

PwMS = People/Person with MS

QOL = Quality of Life

RP = Relapsing Progressive

RR = Relapsing Remitting

RVPFC = Right ventral prefrontal cortex

SD = Semantic Differential

SOPA = Survey of Pain Attitudes

SP = Secondary Progressive

STAI = State-trait anxiety inventory

WCC = Ways of Coping Checklist

I.1) INTRODUCTION

Multiple Sclerosis (MS) is neurological inflammatory disease of a chronic nature involving the central nervous system myelin. MS produces quite a complex array of symptoms. Among these are pain, which may interact with other symptoms such as fatigue, anxiety, depression and cognitive symptoms. These symptoms in combination may have a profound impact on illness perception and illness intrusiveness and may impact overall disability status.

MS is one of the most common neurological diseases in young people, particularly those of northern European origin (McDonald and Ron, 1999). McDonald and Ron note the mean age of onset is generally in the twenties and thirties and that MS is three times as common in women as in men. This gender bias mimics that of other autoimmune diseases (Compston and Coles, 2002).

The spectrum of symptoms include bladder and bowel problems, spasticity, fatigue, pain, sexual dysfunction, sensory disturbance, and balance disturbance (Krupp and Rizvi, 2002). McDonald and Ron (McDonald and Ron, 1999) write that the disease is characterised by exacerbations and remissions with a largely unpredictable course and degree of severity of symptoms and can lead to a complex variety of disabilities. They note that the frequency of relapses varies as well, with the average being 0.8-1.0 per year. Furthermore, certain patients experience a progressive form of the disease from the start.

Diagnosis is based on obtaining evidence of 'dissemination in time and space' of lesions typical of MS as well as clinical, radiological and laboratory evidence (McDonald et al., 2001). MRI is a valuable tool for diagnosis and can be used to identify inflammatory activity and response to therapy (Arnold and Matthews, 2002). The question remains of how to best utilize this diagnostic tool to monitor individual patients.

There is no cure for MS, however disease-modifying drugs do exist. The disease modifying drugs available include: IFN beta-1a, IFN beta-1b, glatiramer acetate and mitoxantrone. These drugs have demonstrated efficacy in relapsing-remitting MS patients by reducing the frequency and severity of relapses and may delay disease progression (Calabresi, 2002). Unfortunately, the efficacy of these drugs has been severely questioned for those with progressive disease. For many people with MS, only symptomatic treatment is available. In addition,

even for those with relapsing disease, these MS therapies have varying degrees of success and may have significant side effects.

I.1.1) ETIOLOGY, PATHOLOGY and PREVALENCE

I.1.1.1) Etiology of MS

It appears that both genes and environment play a role in the development of MS (Poser, 2006). Some specific genetic factors have been found. In monozygotic twins the concordance is only twenty-five to thirty percent (Poser, 2006). The DR2 gene has been under much study as half of MS patients have this gene but so do 15-20% of healthy Caucasians (Wasay et al., 2006). This gene may be a susceptibility gene requiring a second hit by some other factor.

Research to discover the environmental factor(s) have been largely epidemiological. One of the most interesting pieces of the puzzle is that MS incidence increases with increasing distance from the equator (Marrie, 2004). There is also evidence from migration studies that when individuals move from an area of low incidence to an area of high incidence they will adopt this higher incidence. There appears to be a critical age of movement, being pre-adolescence (Marrie, 2004). This can be interpreted as support for a viral etiology or vitamin D hypothesis (Grant, 2006).

Ethnicity also appears to be important. MS is most common in Caucasian populations. MS is more common in women than men, which gives support to the idea that MS has an autoimmune component (Marrie, 2004). The viral evidence comes largely from certain MS 'epidemics'. One notable example was the one in the Faroe islands (Kurtzke and Heltberg, 2001). This epidemic was temporally related to a number of foreign troops being sent to that area related to World War II (Kurtzke and Heltberg, 2001). There are several theories regarding what possible exposure would have occurred with this new population living in this area. These include a change in diet, increase in medical services, and potential exposure to some novel immunological trigger.

One other interesting association is that studies have found that MS relapses tend to happen more in the autumn and spring than in the summer and winter. This may point to an influence of some viral trigger for relapses. Many viruses, both for onset of the disease and as a trigger for relapses, have been explored including measles, influenza, and many members of the herpesvirus

family (Gilden, 2005). If the critical factor is a viral exposure, it may be due to multiple viral exposures, as relatively comprehensive research has been performed on the topic and no single virus has been isolated (Kantarci and Wingerchuk, 2006). It may also just be that different viruses under different circumstances (i.e., timing, combination with a previous virus or virus family, etc) have different outcomes, or that the influence of individual immune responses leads to differing outcomes.

One further complicating factor is the idea that MS itself may be a heterogeneous disease or possibly more than one disease with different etiologies and different disease courses. This would contribute to the difficulty in isolating a viral factor. It may be that a certain virus contributes to a certain subtype and others may contribute to another.

The etiology of MS has not been definitively determined. It is believed that it is likely to be a combination of genetic and environmental causes including viruses. Future research will continue to determine genetic factors. Hopefully future research will also gain more definite results on the influence of environmental factors and be able to identify the factor(s), however this is clearly the more difficult task of the two.

I.1.1.2) Prevalence of MS

It is estimated that MS occurs in 1 in 1,000 people of northern European origin living in temperate climates (Noseworthy, 1999). In the UK, this rate is higher (1.5 in 1000) due to exceptionally high rates in people of Scottish origin and descent (Forbes and Swingler, 1999). In the United States, 250,000 to 300,000 people have MS (Noseworthy et al., 2000) out of approximately 287 million people. Estimated worldwide prevalence of MS of 2.5 million (Compston and Coles, 2002).

I.1.1.3) Pathology of MS

MS is characterised by ongoing central nervous system (CNS) lesion formation leading to cumulative damage (McDonald, 1963). Disease activity can be reversible or permanent. The pattern of relapses and worsening will be described in Section I.1.2. A relapse is an acute event where there is a period of worsening (new symptoms or a worsening of old symptoms). This period is followed by a period of stability with no change in symptoms and then a final

period of recovery (McDonald and Ron, 1999). Recovery can be a return to baseline, incomplete return or no improvement. Most patients experience their second attack 2-3 years after the first. The average relapse rate is one to two relapses every year. Relapse features can predict disease course, with those that are sensory or visual predicting a better course than those that involve cerebellar, motor or sphincter systems (Levic et al., 1999).

A lesion occurs when there is disruption of the blood brain barrier (Minagar and Alexander, 2003). This barrier is designed to protect the brain from pathogenic organisms. A disruption of the blood brain barrier is associated with activation of autoreactive T cells and a resulting cascade of immune system events leading to myelin destruction. The cerebral lesions that are created are discrete plaques of demyelination and can have varying degrees of inflammation (Minagar and Alexander, 2003).

In addition to relapses and progression, there is also subclinical disease activity. Even in areas of 'normal appearing' brain tissue, one can see areas of inflammation, scarring and myelin damage when this tissue is examined under a microscope (Rovaris et al., 2006). Magnetic resonance imaging (MRI) can be used to detect lesions. It has been discovered that most new lesions are not revealed by an onset of symptoms (Pelletier et al., 2001). Lesion burden increases about 5-10% per year (Iannucci et al., 2001). The next phase is brain atrophy and this atrophy reflects axonal loss. Atrophy can be detected even in patients with relatively mild symptoms of the disease (Simon, 1999).

The central nervous system is responsible for motor, sensory, cognitive and psychological behaviour. All of this activity depends on the electrical signalling from one neuron to another neuron. This signalling is carried across on axons and many of these axons are myelinated. The myelin sheath provides insulation for the electric signal ensuring that the signal is fast and accurate. When the myelin sheath is damaged, as in MS, axonal membranes are exposed (Bruck, 2005). This causes the signals being passed on that axon to be lost or at least slowed in their transmission (McDonald, 1963). Demyelinated axons can repair themselves although they do not always do this, and this seems to be the difference between a return to baseline and incomplete recovery. The question

still remains as to why some demyelinated axons do repair themselves and some do not.

Another line of research that found that there is a decrease in MS attacks during pregnancy whereas the postpartum period is associated with an increase in exacerbations (Vukusic and Confavreux, 2006). This may be due to the immunosuppressive state of pregnancy and this lends support to an immune process being responsible for the exacerbations.

I.1.2) MS SUBTYPES

There are four classic subtypes of MS: relapsing remitting (RR), secondary progressive (SP), primary progressive (PP) and benign (BN). This grouping may not always reflect categories easily identifiable in daily clinical practice, but may assist in understanding the patient populations that different studies include. The varying course of disease is accompanied by varying symptom clusters. Pain may co-vary with any of the above disease patterns.

RR is the diagnosis used when a patient has a series of clearly defined neurological relapses with remissions occurring approximately one or two times in two years. Relapses, by definition, last from a minimum of twenty-four hours to several months (Liu and Blumhardt, 1999). In this subtype, there may be either full recovery or some residual disability but with a stable course between attacks (Lublin and Reingold, 1996). RR accounts for approximately 58% of patients overall (Confavreux et al., 1980).

SP is the subtype classification made after there is a transition from RR to a gradual accumulation of disability. The patient undergoes a gradual worsening of neurological impairment with or without distinct relapses (Lublin and Reingold, 1996). The date of onset of the progressive phase can only be determined retrospectively because it requires a 6-month period of progression (Vukusic and Confavreux, 2003a). SP accounts for 24% of patients (Confavreux et al., 1980).

PP patients show a gradual worsening from onset without distinct relapses but possibly with some minor fluctuations (Lublin and Reingold, 1996). Disease onset appears later and the male female ratio is 1:1 (Compston and Coles, 2002). In addition, this form primarily affects the spinal cord and less commonly the optic nerve, cerebrum and cerebellum (Compston and Coles, 2002). PP accounts for 18% of patients (Confavreux et al., 1980).

Some older terms that exist in the literature include Chronic Progressive (CP) and Relapsing Progressive (RP). CP can be interpreted as being PP and RP can be interpreted as being SP.

A patient is diagnosed with benign MS only if there are few relapses with little or no disability during the fifteen years following diagnosis (Lublin and Reingold, 1996). BN accounts for 10 to 20% of patients (Joy and Johnson, 2001).

Fixed disability results from two mechanisms: relapse with incomplete recovery and disease progression (Compston and Coles, 2002). Once walking has been limited to less than 500 meters, the subsequent accumulation of symptoms does not appear to be related to type of initial presentation of the disease (Compston and Coles, 2002).

In the current study, only SP and PP patients will be considered. Differences in these two populations are therefore relevant: age at onset is significantly lower in SP (approximately thirty) than in PP (approximately forty); two-thirds of SP patients are female whereas PP has an equal gender ratio; symptoms at disease onset are also usually different, i.e., visual or sensory symptoms are common in SP onset whereas PP tends to present with spastic paraparesis or hemiparesis; in addition, PP patients progress much more quickly from onset (Vukusic and Confavreux, 2003b). However, Vukusic and Confavreux note there is evidence that the course is similar after a significant degree of disability is reached (Vukusic and Confavreux, 2003a).

I.1.3) SYMPTOMS OF MS RELEVANT TO THIS STUDY

As the range of symptoms in MS is quite wide, the only symptoms that will be discussed at length are pain, depression and anxiety, cognitive issues, and fatigue as they are relevant to the central hypotheses of the study. Research related to these symptoms will be discussed in detail in the following sections. A concluding section will discuss how these issues will be relevant to the current study,

I.1.3.1) Pain

Although pain in MS was first documented by Dr. Jean Martin Charcot in 1875 (Logothetis, 1999), it was not comprehensively examined as a part of the MS experience until the second half of the twentieth century. A classic early

paper, "Pain in Multiple Sclerosis," published in the *Journal of the American Medical Association* (JAMA) in 1973, is written from the perspective of one neurologist who believed that pain was a prominent symptom in MS that was largely ignored (Aring, 1973).

To date there have been relatively few studies looking specifically at pain related to MS. The lack of studies may be due to the heterogeneity of pain syndromes, the varying nature of the disease or to the issues involved in quantifying the unusual pain types that MS may produce.

The official definition of pain, given by the International Association for the Study of Pain (IASP) is "an unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage (Merskey and Bogduk, 1994)." Clifford and Trotter (Clifford and Trotter, 1984) found that it was relatively common to hear a variety of pain reports from MS patients. One third of MS patients who do experience either pain, fatigue, vertigo or paraesthesia describe the symptom as being their worst symptom (Rae-Grant et al., 1999).

In addition to physical pain, there may also be pain with an emotional basis. It is important to note that it was determined, in an experimental pain (non-MS) study, that physical and emotional-based pains share a neurocognitive pathway. Both types of pain produce activation of the right ventral prefrontal cortex (RVPFC). These different types of pain may actually lead to more similar experiences than previously thought (Eisenberger et al., 2003).

Prevalence estimates of pain in MS, show a very wide range, from 13% to 80% (Benrud-Larson and Wegener, 2000). This range may reflect different causes and types of pain in MS (e.g., neuropathic pain, spasticity, postural, headache), a view of different regions of the body (Clifford and Trotter, 1984; Archibald et al., 1994), and whether the pain was major or minor (Goodin, 1999).

I.1.3.1.1) Types of pain in MS

Moulin et al. classified the types of MS pain as acute, chronic or acute and chronic (Moulin et al., 1988): acute pain includes any paroxysmal pain that is generally considered to be symptomatic of demyelinating disease and includes trigeminal neuralgia, L'hermitte's sign, paroxysmal burning pain and painful tonic seizures; chronic pain presents either intermittently or continuously over a period

of at least one month and does not have another obvious non-MS cause and includes dysesthetic extremity pain, back pain and painful leg spasms; some patients experience a combination of acute and chronic pain symptoms (Moulin et al., 1988).

I.1.3.1.2) Prevalence of pain in MS

Carter et al. looked at the types of symptoms people experienced overall and within the initial presentation (Carter et al., 1950). An estimated 28% of MS patients suffer from pain when taken as a current status or point prevalence (Gebhart et al., 1994; Wall and Melzack, 1999) however disease course prevalence has been found to be much higher, closer to 67% (Rae-Grant et al., 1999). Moulin reports that 55% of patients suffered from pain at some point in the course of their disease (Moulin et al., 1988; Moulin, 1989). Of patients who experienced pain, 48% experienced chronic pain.

Many studies have tried to determine an accurate prevalence rate based on patient self-report. Prevalence rates vary considerably, which may be explained in terms of different subgroups of pain in MS and different methodologies (assessment techniques, time frames, inclusion/exclusion of pain types, and possibly data collection). Details of pain prevalence by study are presented in Table I.1.3.1.2.A-I.

TABLE I.1.3.1.2.A) PREVALENCE OF PAIN IN MS (PAGE 1 OF 9)

Study	Number of patients	Exclusions	Data Collected	Prevalence per total #	Correlations	QOL
(Archibald et al., 1994)	85 Outpatients (13M, 72F) Age:19-75 (mean 41.5) RR: 40%, RP: 26% CP: 29% BN: 5%	NONE	EDSS, Mental Health Inventory (MHI), structured pain interview.	Overall: 52.9% RR: 41.7% RP 54.4% CP 52% B 100% By region Head 53.3% trunk 48.9% arm 57.8% leg 73.3% > 1 region 76%	Both disease duration and neurologic severity corr w/pain hours/week but not w/ pain severity or number of pain sites or pain related distress Age was not correlated with any pain variable all at the $p<0.05$ criterion	56% of those reporting pain stated their ability to perform as worker was reduced by 50%
(Buchanan et al., 2001)	9013 admission assessments for a nursing home	NONE	Minimum Data Set (MDS) administered to residents upon admission to a nursing home	Overall:50.8% By region soft tissue/lesion/muscle 30.3% back 24.5% joint (other than hip) 23.6% Frequency: Daily pain:28.8% Non-daily pain: 22% Severity: mild pain: 27.9% moderate pain: 57.6% severe pain:14.5%	Did not compute correlations between pain and any other variable	NONE

QOL= Quality of Life

TABLE I.1.3.1.2.B) PREVALENCE OF PAIN IN MS (PAGE 2 OF 9)

Study	Number of patients	Exclusions	Data Collected	Prevalence per total #	Correlations	QOL
(Carter et al., 1950)	46 out of 393 pts at hospital patients	Only included autopsy-verified cases	Examined records indicating pain	Overall: 42% By region: one arm: 4% one leg: 11% both legs: 11% trunk: 7% face: 7% Initial symptom only: 23.9% By region one arm: 0% one leg: 4% both legs: 2% trunk: 4% face: 2%	NONE	7% of patients underwent remissions which consisted of improvement in pain

TABLE I.1.3.1.2.C) PREVALENCE OF PAIN IN MS (PAGE 3 OF 9)

Study	Number of patients	Exclusions	Data Collected	Prevalence per total #	Correlations	QOL
(Clifford and Trotter, 1984)	317 pts at research MS clinic using a medical records audit	Patients concomitant diagnosis of conversion symptoms or hysteria Pain Headache and pain that was relieved by OTC analgesics were excluded	Examined records indicating presence of pain for more than 2 weeks	Overall:28.8% By region Burning extremity 20% non-specific limb 16.5% back 7.7% root 7.7 joint 6.6% By type painful extremity spasm 6.6% myalgias and cramps 5.5% optic neuritis 5.5% face or head neuralgia 5.5% painful L'hermitte's sign 5.5% thoracic 4.4% back w/ nonspec. leg pain 3.3% back w/ sciatica 2.2% nonburning dysesthesias 2.2% electric shock in limbs 2.2% neck pain 1.1%	Age range and pain percentage: 15-20 - 12.5% 21-25 - 16.7% 26-30 - 22.5% 31-35 - 35.8% 36-40 - 39.1% 46-50 - 22.9% 51-55 - 32.1% 56-60 - 42.1% 61-65 - 63.6% 66-70 - 60.0% Duration of disease (yr) correlations: 0-5 - 22% 6-10 - 39% 11-15 - 29% 16-20 - 22% 21+ - 52%	NONE

TABLE I.1.3.1.2.D) PREVALENCE OF PAIN IN MS (PAGE 4 OF 9)

Study	Number of patients	Exclusions	Data Collected	Prevalence per total #	Correlations	QOL
(Ehde et al., 2003b)	442/1453 people returned survey from an MS Association list	NONE	Novel questionnaire regarding pain over the past three months and a numerical rating scale	44% reported persistent, bothersome pain. 51% of these reported that this pain only mildly interfered with daily activities. 20% said it severely interfered with daily activities.	Those who had pain had more severe MS, were more likely to be receiving disability benefits, more likely to report decreased activity, including household activities than those without pain.	Of those with pain, 27% described it as significant or their most significant problem.
(Goodin, 1999)	168/493 patients returned questionnaire from a MS society list Respondents RR: 58% SP: 22.6% PP: 20.1%	NONE	Novel questionnaire where subsets were converted to an EDSS score, neurologic rating scale (NRS), ambulation index (AI) and mean disability scale (MDS)	Overall: 61.9% Patients were divided into major pain and minor Minor pain 42.3% Major pain 19.6%	NONE	18.3 % w/ minor pain and 36.4% w/ major pain have been treated.

TABLE I.1.3.1.2.E) PREVALENCE OF PAIN IN MS (PAGE 5 OF 9)

Study	Number of patients	Exclusions	Data Collected	Prevalence per total #	Correlations	QOL
(Moulin, 1989)	159 patients at MS clinic in a Univ hosp. 62% clinically definite MS 38% possible /probable MS	Patients Those in chronic care facilities were excluded Pain Headache or pain relieved by aspirin,	Questionnaire followed by interview and EDSS	Overall:55% Acute 9% incl: trigeminal neuralgia 4.4% L'hermitte's sign 2.5% tic-like extremity 1.3% tonic seizures 1.3% Chronic 47% , incl: dysesthetic extremity 29% back 14% leg spasms 13% visceral 2% Both acute and chronic 2%	Gender:Women more likely than men (3:1 pain, 1.4:1 no pain) Age: More common w/ increasing age. 20-30 – 40%; 31-40 - 49%; 41-50 - 59%; 51-60 - 64%; 60+ - 73% Disease duration: More common if duration of disease more than 5 yrs 0-5 - 30%; 6-10 - 63%; 11-15 - 53%; 16-20 - 59%; 21+ - 68% NO effect: age of onset, duration of disease, presence of myelopathy, degree of disability (EDSS)	NONE

TABLE I.1.3.1.2.F) PREVALENCE OF PAIN IN MS (PAGE 6 OF 9)

Study	Number of patients	Exclusions	Data Collected	Prevalence per total #	Correlations	QOL
(Osterberg et al., 2005)	364 MS patients	Pain Central only included	Novel questionnaire about pain & sensory symptoms	Overall: 28%	NONE	NONE
(Rae-Grant et al., 1999)	224 pts with MS (28%M, 72%F) RR, SP, PP, B 93 healthy controls (matched by age/sex) obtained from neurological practices	NONE	Self-designed survey with questions about demographic data, disease duration, disability, memory, pain, etc.	Overall: 67% at some point in disease course. 44% of these patients had active pain problems. Controls had the same percentage of pain but fewer (22%) had active pain problems.	No correlation with disease duration or disability as stated by individual.	5% described pain as their worst symptom 10% described paresthesias as their worst symptom.

TABLE I.1.3.1.2.G) PREVALENCE OF PAIN IN MS (PAGE 7 OF 9)

Study	Number of patients	Exclusions	Data Collected	Prevalence per total #	Correlations	QOL
(Stenager et al., 1991)	117 MS inpatients then were divided into: Without pain, chronic pain or acute pain.	Patients if had they had another CNS disease or additional chronic disease	A neurological exam, neuropsychological testing, a questionnaire and a structured interview	Overall Without pain 35% at one point 65% at the time of investigation 45% at onset 23% By region dysesthesia 17% low back 9.5% spasms and tonic seizures 34% extremity tension 34% L'hermitte's sign 3.8% neuralgia 1.2%		

TABLE I.1.3.1.2.H) PREVALENCE OF PAIN IN MS (PAGE 8 OF 9)

Study	Number of patients	Exclusions	Data Collected	Prevalence per total #	Correlations	QOL
(Svendsen et al., 2003)	627/771 MS patients, contacted by mail survey and 487/769 non-MS controls	Patients must have definite diagnosis Controls Matched by sex, age and locality.	A questionnaire regarding pain in the past month (acute and chronic)	In MS: 79.4% presented with pain By region: Extremities: 50% Joints: 45% Back:43% Head: 41% Muscles: 40% Neck: 33% Eyes: 20% Abdomen: 19% Chest: 12% Face: 11% In controls: 74.7% presented with pain (*no signif. diff)	In MS: Highest prevalence of pain in group aged 40-59. Compared to controls: In over 70, there was signif. diff between MS v controls. More MS patients reported moderate-severe pain More MS patients reported daily or constant pain More MS patients reported using physiotherapy and using more analgesics. More MS patients reported pain in more than one location	NONE

TABLE I.1.3.1.2.I) PREVALENCE OF PAIN IN MS (PAGE 9 OF 9)

Study	Number of patients	Exclusions	Data Collected	Prevalence per total #	Correlations	QOL
(Vermote et al., 1986)	83 MS patients, hospitalized for rehab	Patients Must have pain (n=45) Pain headache or visceral pain	McGill and EDSS	Overall: 42% presented with pain	All patients had an EDSS 3 to 9. Slight increase in frequency of pain was seen with increasing disability although tendinoskeletal pain (capsulitis & osteoarthritic pain) was more frequent when there was need for assistance in walking.	NONE

I.1.3.1.3) Assessment

Pain in the MS population, is most often neuropathic rather than sharp, muscular pain (Rae-Grant et al., 1999). Although trigeminal neuralgia and muscular spasm probably would be identified by typical pain assessment, additional symptoms, that meet the official definition of pain, are missed by such assessments. Overall pain assessment is difficult because the overwhelming majority of measurements are designed to detect sharp, muscular pain. This difficulty in assessing pain explains the importance of the validation of the McGill Pain Questionnaire (Melzack, 1975) and the identification of pain subtypes (Vermote et al., 1986).

I.1.3.1.4) Etiology

Pain may be caused by many different and interconnected factors: the inflammatory demyelinating process, spasm or other musculo-skeletal factors directly or indirectly related to demyelination, and even the drugs used to modify the immune system or symptoms, among many others. In addition, neuropathic pain may result directly from damage to the nervous system (peripheral nerve, dorsal root ganglion or dorsal root, or the central nervous system (CNS)) (Woolf and Mannion, 1999).

Some of the postulated causes of pain and the details of the way in which these may lead to pain will be reviewed in the following section. In general, the basic pathology of the inflammatory process in MS leads to partially demyelinated axons which conduct impulses at a slower velocity and can also discharge spontaneously (Compston and Coles, 2002). The inflammatory process of MS involves demyelination and may lead to either positive or negative symptoms (Moulin et al., 1988). A positive symptom is one which results from unwarranted spontaneous nerve signals leading to symptoms like dysesthesia or painful tonic seizure (Sakurai and Kanazawa, 1999). Tonic seizures are associated with muscle cramping and spasms (Maloni, 2000). Negative symptoms result from a conduction block along a demyelinated part of a nerve fibre which may lead to paresis or hypesthesia (Sakurai and Kanazawa, 1999). Both may produce pain symptoms.

Patients may experience acute pain syndromes spontaneously or with tactile stimulation or movement in an involved limb (Moulin et al., 1988). The

types of pain this can produce include: tic-like extremity pain, burning dysesthetic pain or painful tonic seizures among others (Moulin et al., 1988). Patients with weak limbs may experience pain specifically due to prolonged immobility (Moulin, 1998) particularly of ulnar and peroneal palsies (Moulin et al., 1988).

Classic pain syndromes that are reported within the MS patient population include the pain associated with optic neuritis and painful tonic spasm. The pain associated with optic neuritis supposedly occurs due to stretching of the meninges surrounding a swollen optic nerve (Moulin et al., 1988). Trigeminal neuralgia causes a sensation of brief electric shock-like pains and is due to a demyelination in the proximal part of the trigeminal nerve root (Love et al., 2001). Trigeminal neuralgia, although only seen in 2% of MS patients, is still four hundred times more common in MS patients than in the general population (Maloni, 2000). Episodic facial pain as a precursor to trigeminal neuralgia has been observed in MS patients (Rashbaum et al., 2003). Painful tonic spasm is the experience of rapid onset, muscle spasms (Joy and Johnson, 2001). Spasticity is a major risk factor for spasm and spasticity is principally caused by an upper motor neuron causing disinhibition of spinal reflexes (Sheean, 2001). Headache is another painful symptom. It has been observed with a higher frequency in MS patients than in the general population (Evans and Rolak, 2001) however, the headache and MS relationship is still under debate (Rashbaum et al., 2003).

There is debate over whether pain in MS is related of disease duration. One study found that disease duration was significantly correlated with pain hours per week (r=0.303, $p<0.05$) but not with pain severity (r=0.014, $p>0.05$), number of pain sites (r=-0.053, $p>0.05$) or pain related distress (r=0.002, $p>0.05$) (Archibald et al., 1994). In a different study, incidence of pain significantly varied with disease duration, peaking during the second five years and after twenty years ($p<0.01$) (Clifford and Trotter, 1984). Other studies have found no correlation between mean disease duration and pain but found that there was significantly more pain if disease duration was longer than five years ($p< 0.01$) (Moulin et al., 1988; Moulin, 1989). Some studies found a slight but insignificant increase in pain with disease duration ($p>0.05$) (Stenager et al., 1991). Others have found no significant correlations between disease duration and pain

(p=0.54) (Rae-Grant et al., 1999). It appears that the issue of the relationship between disease duration and pain experience is still unresolved.

There is also debate over how level of disability may relate to pain experience. One important factor may be the way in which disability is classified. Broadly, disability may be determined by the neurologist using the Expanded Disability Status Scale (EDSS) (Kurtzke, 1983) or another measure or subjectively by the patient. Although logically one may expect pain to be related to level of disability, this has not always been supported in empirical study. This lack of correlation between measures of pain and disability may be related to the properties of the scales used (see 'Explanation of EDSS' in the following paragraph). Most studies use the EDSS score as a measure of disability. Current commonly used measures are not capable of quantifying and describing these two complex factors with sufficient precision to elucidate an association between them.

The majority of the relevant studies used the same assessment of disability, the EDSS. Many reservations have been expressed about this measure. These issues will be reviewed before specifically considering the experimental investigations of the relationship between pain and disability.

The EDSS is the most common measure of disability and impairment used within the MS population, however it has acknowledged shortcomings (Hobart et al., 2000). One of the criticisms of the DSS (predecessor to the EDSS) is that it was too limited in its middle range for studies of 'chronic MS (Hobart et al., 2000). As a result, the DSS was subdivided into two separate steps. This was not sufficient to allay criticism, but the EDSS continues to be the most widely used disability measure for the MS population in clinical trials (Hobart et al., 2000).

Hobart et al. specifically analyse the measure by its psychometric properties. Acceptability (the distributions of scores) of the EDSS was measured against the Barthel Index (BI) and the Functional Independence Measure (FIM). The BI and FIM showed superior acceptability (Hobart et al., 2000). Reliability (intra- and inter-rater reliability) was tested and showed that different rater's scores varied by approximately 2 EDSS points. Validity (precision of measurement allowing discrimination of individuals) studies showed that the EDSS had the least ability to discriminate between patients in terms of disability.

Responsiveness (effect size) studies showed that the EDSS has the poorest ability to detect change. From a psychometric standpoint, the EDSS is not the best measure of disability available.

Recognising the weaknesses of the EDSS measure, the experimental evidence for the relationship of pain to disability will now be discussed. Some studies have not found degree of disability to predict pain when comparing an MS pain group to an MS non-pain group (Moulin et al., 1988; Moulin, 1989). However, three-quarters of all patients in these studies were ambulatory and therefore the range of disability in the sample is not representative of the range of disability in the entire MS population. Nortvedt et al. found that EDSS scores were not correlated with bodily pain as assessed by SF-36 pain question scores (r=-0.09, $p>0.05$) (Nortvedt et al., 1999). However, Archibald et al. (1994) found disability to be correlated with pain hours per week (r=0.322, $p<0.05$) but not with pain severity (r=0.149, $p>0.05$), number of pain sites (r=-0.0118, $p>0.05$) or pain related distress (r=0.131, $p>0.05$). Several studies have found slight increases in pain with disability as assessed by EDSS ($p>0.05$) (Vermote et al., 1986; Stenager et al., 1991). In particular, Vermote et al. found an increase in reports of 'tendinoskeletal pain' when the EDSS > 6, (unaided walking is not possible, was found.

Studies looking at the correlation between disability and pain used the EDSS almost exclusively although at least one study used a different measure of disability. Rae-Grant et al. (Rae-Grant et al., 1999), asked the patients to say if they were disabled (yes or no answer) and also asked these patients separately about pain (whether they had ever experienced pain and whether they were actively experiencing pain). They found no correlation between self-reported disability and pain ($p=0.88$). However, they did find that number of sensory symptoms and disability were correlated ($p<0.001$).

Given the preceding data, it appears that disability, particularly if using the EDSS, is not generally correlated with pain. However, it is possible that pain and disability are linked only in certain types of patients. For example, patients who are wheelchair-bound, with a lack of muscle control may experience awkward seating, possibly leading to chronic back pain. This type of pain would be

classified as muscular pain. However, pain may also be of a neuropathic etiology (Sakurai and Kanazawa, 1999).

In summary, pain in MS does not generally have a simple relationship to disability, at least using the EDSS measure. The EDSS is unlikely to disappear as a disability measure because it is a widely utilized and familiar rating system and is useful for mobility status. However, it is possible that if one were to look at specific subtypes of pain or use different assessments for disability and/or pain, a relationship between pain and disability might be observed. The current study may have the ability to determine the true nature of a relationship between disability and pain in MS, if there truly is a relationship. In this study, the study sample is a much more disabled population than those considered in most research studies and although the EDSS is used, there are additional patient report measures addressing disability.

I.1.3.1.5) Treatment

I.1.3.1.5.1) *Pharmacological therapy for pain*

Traditional prescribed pain management medications include opioids and muscle relaxers. In addition, different chronic pain populations have used cannabis, although much of this use was without medical support.

Available treatments for pain specifically in MS include primarily carbamazepine, phenytoin and tricyclic antidepressants. Carbamazepine has antiepileptic, neurotropic and psychotropic properties and is a dibenzazepine derivative (Toosy and Thompson, 2000). Phenytoin is usually used as an anticonvulsant but is successful as a treatment for neuropathic pain (Toosy and Thompson, 2000). Tricyclic antidepressants, such as imipramine and amitriptyline, have also been found effective for neuropathic pains such as uncomfortable sensation and burning extremity pain (Sindrup and Jensen, 1999; Toosy and Thompson, 2000).

In general, types of medications specifically for neuropathic pain have not been universally effective. Although, it has been shown that although neuropathic pain is not completely alleviated by opioids, opioids do have some effect on pain (Kalman et al., 2002). Traditionally, anticonvulsants (e.g., phenytoin and carbamazepine) and antidepressants (e.g., amitriptyline) have been used with the intention of creating a non-specific CNS depression, however,

these also tend to have many unwanted side-effects (Dickinson et al., 2003). As a result, new anticonvulsants (lamotrigine and pregabalin), antidepressants (Selective 5-HT reuptake inhibitors and bupropion), Ca2+ channel modulators and NMDA receptor channel modulators have been used with better side-effect profiles (Dickinson et al., 2003).

An earlier study stated that one of the treatments available for neuropathic pain was tricyclic antidepressants (Clifford and Trotter, 1984). This study attempted to assess pain syndromes in MS, however, the group excluded pain which was a symptom of paresthesia and any minor pain which may be relieved by over the counter analgesics or which did not last for at least two weeks.

One study by Heckman-Stone and Stone (Heckman-Stone and Stone, 2001) looked at people with MS and the types of treatments they found effective. Medications were cited as being the most effective therapy. However, additional effective therapies included physical/thermal manipulation, exercise, psychosocial and alternative therapies.

For relieving the pain related to spasticity, a multi-professional approach has been suggested, specifically, the type of therapy should be based on the patient's condition and overall health needs (Ward and Kadies, 2002). The authors note currently available treatments include: oral pharmacological therapy, local pharmacological therapy, motor point blocks, botulinum toxin therapy or intrathecal agents as well as surgical interventions.

I.1.3.1.5.2) Percentage that get treated

There are some pharmacotherapeutic approaches that seem to improve symptoms, but do not alleviate all pain in all instances and may not be available to all patients. Only 41.5% of MS patients with pain had ever been treated for their pain (Stenager et al., 1991). Similarly in a study conducted on individuals recruited through the Northern California MS Society, just over half (54.7%) of patients who had either minor or major pain had ever received treatment for their pain (Goodin, 1999).

I.1.3.1.5.2) Treating contributory factors

It has been shown that distress is significantly correlated with pain in MS (Archibald et al., 1994) however, interventions for pain-related distress have not been fully explored. For the purpose of the current study, distress is the term

used to describe the intrusion and avoidance of thoughts and feelings that relate to pain, depression, anxiety and MS (Janssens et al., 2003a). As these symptoms are often behaviourally indistinguishable, it is necessary to consider all together (Berde and Wolfe, 2003).

One method that has been used for treating pain in combination with other sustaining factors is cognitive behavioural therapy (CBT). Williams et al. looked at cognitive behavioural therapy for pain management, in both an inpatient and outpatient setting for general pain management in a mixed group (Williams et al., 1996). Participants were randomly assigned to one of three treatments: inpatient pain management, outpatient pain management or waiting list control. The types of behaviours that were addressed were exercise and stretching, goal setting, pacing of activities, education about pain (treatments, maintenance of changes, identification of pain cues, etc.), drug reduction counselling, relaxation training, sleep management, crisis management with a family involvement component. Williams et al. found both treatment groups with mixed chronic pain improved (over waiting-list controls) in terms of psychological distress, pain behaviour, health related disability and pain intensity. Inpatients made greater strides in all physical measures as well as pain impact, depression, pain self-efficacy, catastrophising (defined in Section I.2.4), hopelessness and anxiety (these issues will be defined and addressed in depth in later sections). Cognitive behavioural therapy has been effective as well in a heterogeneous chronic disease population for reducing distress, reducing physical symptoms and improving health related quality of life (HQOL) (Reibel et al., 2001).

I.1.3.2) Depression and Anxiety

I.1.3.2.1) Types

Anxiety and depression can occur separately or in combination. In MS, depression when it occurs, is more commonly found in combination with anxiety; whereas anxiety is found to occur more commonly alone (Feinstein et al., 1999).

I.1.3.2.2) Prevalence

Depression is the most common psychiatric condition found in people with neurological conditions (Chang et al., 2003). MS patients have a relatively high lifetime prevalence for major depression (Feinstein and Feinstein, 2001). Seventeen percent of patients were diagnosed with major depression, with a

lifetime depression prevalence of 15% to 50% (Feinstein and Feinstein, 2001). An additional 50% of Feinstein and Feinstein's study participants displayed individual symptoms without meeting the full criterion for a diagnosis of major depression. Sadovnick et al. found the actual lifetime prevalence of depression in MS to be 34.4% with an estimated lifetime prevalence by age 59 of 50.3% (Sadovnick et al., 1996).

It may be understandable for people with a chronic disabling disease to have a higher rate of depression when compared with healthy controls. However, the rate of depression in people with MS is higher than for people with other chronic disabling diseases (Sadovnick et al., 1996). As a point of reference, psychiatric disorders have an overall rate in the general population of 17.5% in the past six months and 33.0% lifetime prevalence. In people with one or more medical conditions, the rate goes up to 24.7% and 42.2% respectively (Wells et al., 1988).

Anxiety is also relatively common in the MS population (Feinstein et al., 1999). Feinstein et al. found 25% of patients had clinically significant anxiety, a rate three times that for depression in the same study. In addition, patients' symptoms of anxiety and depression often went unrecognised and untreated. MS patients with clinically significant co-morbid psychological symptomatology (anxiety and depression) were no more likely to be taking psychotropic medication than MS patients with either anxiety or depression alone unlike the primary psychiatric population where those with co-morbid anxiety and depression were more likely to seek and be given treatment.

Prevalence of anxiety and depression also differs by MS subtype. The PP subtype may be less likely to experience depression and/or anxiety than the SP subtype (Vleugels et al., 1998).

I.1.3.2.3) Assessment

Commonly used measures for hospital populations to assess anxiety and depression are the Hospital Anxiety and Depression Scale (HADS) (Zigmond and Snaith, 1983) and the General Health Questionnaire (GHQ) (Goldberg, 1972). The HADS is designed for use with medical populations and has 2 subscales (anxiety and depression) with 7 questions each (anxiety-related questions alternating with depression questions) (Zigmond and Snaith, 1983). Scores from

8-10 are taken to indicate borderline anxiety or depression respectively and scores greater than 10 on either subscale are taken to indicate anxiety or depression respectively. The GHQ consists of 28 items and contains 4 subscales of anxiety, depression, social dysfunction and somatic difficulty (Goldberg, 1972).

Chang et al. developed the Chicago Multiscale Depression Inventory (CMDI) on the basis of a study done to identify the differences between depression in MS versus symptoms of depression in other situations (Chang et al., 2003). Some common signs of depression like fatigue are primary physical symptoms of MS present in psychologically healthy people with MS. Therefore it is necessary to use a measure that accounts for the specific underlying disease so there is not an over estimation of depression in this sample.

An additional issue is whether depression is a reaction to the disease or a product of primary pathology (Chang et al., 2003). This issue will be discussed further in the 'Etiology' section. However, the CMDI was developed in order to differentiate the experience of depression separately from the experience of MS. Chang et al. found that the endorsement of statements such as 'I feel useless' was predictive of depression and 'I feel tired' or 'I feel sluggish' was not predictive in this population. This is different than in the general population in which all items may be predictive of depression (Chang et al., 2003).

I.1.3.2.4) Etiology and links to other disease variables

Patients with clinically significant anxiety (HADS>10) did not have a longer duration of disease or degree of disability and female MS patients were more prone to develop anxiety than males, even for those with similar disease profiles (Feinstein et al., 1999).

There is some evidence that depression may be organic sequelae of MS. Depression may occur as a result of increased cytokine release which seems also to be a causative factor in MS relapse or progression (Pollak et al., 2002). Results of the Beck Depression Inventory have been correlated with interferon gamma production (Mohr et al., 2001). Lynch et al. found that depression was linked to disability. This link did not appear to be mediated by coping or other psychological variables, and organic depression may be a result of neurological damage (Lynch et al., 2001).

I.1.3.3) Cognitive Issues

I.1.3.3.1) Types

The most common types of cognitive impairment appear to be in attention, memory, abstract reasoning, speed of information processing and executive functioning (Rao et al., 1993b; Rao et al., 1993a; Langdon and Thompson, 1999). General intelligence and language are less likely to be affected (Rao, 1995). Cognitive impairment is significant because it has been shown to impact on social activities (Rao et al., 1991), mood (Gilchrist and Creed, 1994) and overall disability (Beatty et al., 1995). Tests of cognitive function must be validated on an MS study group if they are to be used effectively in this population (Arnett et al., 1999b; Higginson et al., 2000).

I.1.3.3.2) Prevalence

Cognitive impairment rates in outpatient and community samples range from 30% to 70% (Krupp and Rizvi, 2002). For 20% of people with MS (PwMS), cognitive impairment is significant enough to disrupt function in work or family life (Rao et al., 1991).

There have only been weak correlations between cognitive performance and degree of physical disability (Peyser et al., 1990). Cognitive impairment is not generally found to be significantly correlated with illness duration, disease course, depression or medication usage (Rao et al., 1991). Depression can adversely affect performance on neuropsychological testing but only for tasks that challenge working memory capacity (Arnett et al., 1999a; Arnett et al., 1999b; Benedict et al., 2002).

Cognitive impairment appears to be more severe for SP MS individuals than for RR MS individuals (Feinstein et al., 1992). This difference may be most noticeable when using measures testing the working memory capacity (Archibald and Fisk, 2000). Some studies have found the level of cognitive impairment also to be more severe in SP MS than in PP MS (Comi et al., 1995) but not all (Foong et al., 2000). There are significant differences between the RR, SP and PP groups in terms of the overall lesion burden with the SP groups generally showing the most extensive burden of the three groups (Thompson et al., 1990) which might lead to the expectation of greater cognitive impairment for those with SP MS. Although there may be connections between MS subtype and cognitive

impairment, subtype and disease duration do not accurately predict cognitive ability in individual patients (Beatty et al., 1990).

I.1.3.3.3) Assessment

Thoroughness of cognitive assessment is particularly important as one half of MS patients with documented impairment based on a neuropsychological assessment were found to be cognitively normal using standard screening during neurological examinations (Beatty and Goodkin, 1990). Generally, MS patients are not routinely assessed using neuropsychological testing which includes measurements of processing speed, working memory, learning memory, word retrieval, visual-spatial processing and executive functioning i.e., abstract reasoning, conceptual framework and planning and organization of behaviour (Benedict et al., 2002).

Assessment measures of cognitive functioning must be carefully selected to minimize visual or motor disturbances on the measure. Past studies examining cognition have failed to control for potential confounding variables such as depression, work history and physical disability (Feinstein et al., 1992). Practice effects are also common in neuropsychological testing and must be considered (Benedict et al., 2002).

I.1.3.3.4) Etiology

Impaired neural transmission may reduce information processing efficiency and be the basis for the various cognitive problems in MS (Archibald and Fisk, 2000). Cognitive deficits show a correlation with overall MR lesion burden (Hohol et al., 1997). However, the overall lesion burden imperfectly predicts the amount of cognitive impairment (Camp et al., 1999; Foong et al., 2000). Lesions of the (juxta)cortical type were more useful at predicting neuropsychological impairment than total lesion burden (Lazeron et al., 2000). Some specific cognitive deficits have been correlated with specific lesion location (Krupp and Rizvi, 2002). Another technique, magnetisation transfer histogram analysis has more recently been used to assess functioning of normal appearing brain tissue (Miller et al., 2003). It is suspected that not all brain tissue that is lesion free on MRI is truly healthy tissue. This technique may be capable of further defining the pathological processes causing cognitive impairment in MS patients.

Brain atrophy has been found to be a relatively useful predictor of cognitive deficits with central atrophy being strongly associated with poor neuropsychological outcome (Benedict et al., 2004). However, atrophy of the corpus callosum is more important that whole brain atrophy with regard to cognitive impairment. MRI of the corpus callosum has been used for this identification purpose and shows mental processing speed and rapid problem solving may be affected. Smaller size in part of the corpus callosum may lead to fewer callosal fibres, decreased interhemispheric transfer and be useful as an early sign of probable cognitive deficit (Pozzilli et al., 1991).

The longitudinal pattern of deficit is very interesting and well documented. If there are early cognitive impairments, it is likely that the patient will acquire further impairments. If there are no early impairments, it is likely the patient will remain cognitively stable over next 3 years (Kujala et al., 1997). Amato et al. looked at a cohort of MS patients assessed after diagnosis and reassessed again after 10 years (Amato et al., 2001). They found that 20 of the 37 patients, who were cognitively unimpaired at the start of the study, remained so after 10 years.

I.1.3.3.5) Pharmacological Treatment for Cognitive Impairment

Treatments for general cognitive deficits have been attempted. However, pharmacological therapies have shown limited benefit to date. Two available pharmacological therapies are Donepezil Hydrochloride and 4-aminopyridine. MS patients with moderate to severe cognitive impairment who were treated with Donepezil Hydrochloride showed significant clinical improvement (Greene et al., 2000). Similar patients treated with 4-aminopyridine showed a trend in improvement but not a significant difference pre and post treatment (Smits et al., 1994). Amantadine and pemoline also did not show significant benefit for cognitive functioning (Geisler et al., 1996). Interferon therapies have been explored for their ability to aid in the maintenance of cognitive function. Some studies have shown a significant beneficial effect (Fischer et al., 2000; Barak and Achiron, 2002) however, other effects of interferon therapies (increased fatigue and mood symptoms) may lessen its functional benefit.

I.1.3.4) Fatigue in MS

I.1.3.4.1) Types

There appear to be three clinically different effects of fatigue: asthenia (a condition of weakness, usually arising from muscular or psychological disorders), fatigability (fatigue with exercise) and the worsening of symptoms with effort (Iriarte et al., 2000). Fatigue is characterized as a feeling of tiredness or lack of energy. One of the signs is reduced effectiveness in a function as time passes; for example, it is possible to have specific symptoms of muscle or visual fatigue (Iriarte et al., 2000). Fatigue in MS is an abnormal sense of tiredness, which is disproportionate with degree of exertion and interferes with daily life. Fatigue within MS can also impact on cognitive functioning (Krupp and Elkins, 2000).

I.1.3.4.2) Prevalence

Fatigue is a frequent symptom in people with MS and appears to occur in 76% to 85% of patients (Giovannoni et al., 2001). Sixty-nine percent of MS patients reported that fatigue was either their worst of one of their worst symptoms (Fisk et al., 1994) and 28% reported it was their worst symptom (Krupp et al., 1988).

I.1.3.4.3) Assessment

Measurement of fatigue can be accomplished with one of the assessments for fatigue, validated in MS patients, including the Fatigue Descriptive Scale (FDS) (Iriarte et al., 1999) and the Krupp Fatigue Severity Scale (KFSS) (Krupp et al., 1989). In choosing an assessment, it is important to take into consideration the interaction between different symptoms. Many MS symptoms can increase fatigue. Physical conditioning, pain, sleep, mood, heat exposure and medication should all be considered when assessing fatigue (Krupp and Rizvi, 2002).

I.1.3.4.4) Etiology

There may be different mechanisms for fatigue in MS including neurological deficits, lack of sphincter control (causing frequent waking during the night), sleep disorders, medications, endocrine alterations as well as psychiatric and psychological problems (Iriarte et al., 2000). These symptoms are simply possible causes as none have been shown to be definite causes. Several

studies have found that fatigue significantly predicts depressed mood in MS independent of physical disability (Randolph et al., 2000; Voss et al., 2002).

Some suggested mechanisms for fatigue in MS are changes in neurotransmitters, a disruption of the pathways leading to arousal and decrease in the availability of some amino acids (Krupp and Rizvi, 2002). Using immunological markers, it has been demonstrated that the proportion of patients with fatigue was significantly higher for those with apparent immunoactivation than for those with normal immune status (Iriarte et al., 2000). MS patients with no fatigue have been shown to have more activation (using functional magnetic resonance imaging (fMRI)) in cortical areas devoted to motor planning and execution in the ipsilateral cerebellar hemisphere, ipsilateral precuneus, ipsilateral rolandic operculum, the contralateral middle frontal gyrus and the contralateral thalamus (Filippi et al., 2002). MS patients with fatigue have more significant activation of the contralateral cingulated motor area (Filippi et al., 2002).

Examining the possible correlations between fatigue scales, Giovannoni et al. found that the Fatigue Questionnaire Scale (FQS) did not correlate with the KFSS (r=0.08) or with the Hospital Depression Scale (HDS). The FQS correlated negatively with the Hospital Anxiety Scale (HAS) (r=-0.62), which in itself, it counterintuitive. The KFSS did not correlate with either the HAD or the HDS (Giovannoni et al., 2001). Given these data, it appears that each fatigue scale examines different areas that fatigue may impact. One must be cautious in choosing which fatigue scale to use in research with this population.

It is important to examine the correlations between fatigue and other symptoms as fatigue may the cause or the result of these other symptoms. Fatigue is significantly related to level of disability and not related to subtype of MS after controlling for disability status (Kroencke et al., 2000). Iriarte at al. found that patients with fatigue had significantly higher scores on the Kurtzke scale in the pyramidal and global EDSS coefficient than the non-fatigue group ($p<0.001$) (Iriarte et al., 2000).

In addition to depression mimicking fatigue, there appears to be a significant correlation between fatigue and depression even when all overlapping items are eliminated from scales used to measure depression (Kroencke et al.,

2000). Patients with fatigue also had a higher degree of anxiety than did those without fatigue (Iriarte et al., 2000). Depression, anxiety, and sleep disorders had a high positive predictive value and specificity for fatigue (Iriarte et al., 2000).

Fatigue associated with MS should be differentiated from fatigue associated with depression. In differentiating MS related fatigue from depression related fatigue, MS related fatigue is aggravated by heat, is often alleviated by sleep, and lasts for a few hours as opposed to the persistent fatigue associated with depression (Patten and Metz, 2000).

I.1.3.5) Quality of Life

Quality of life is becoming an increasingly appreciated issue. A recent population based study examined 185 people with MS (Pittock et al., 2004) who reported a worse quality of life for the aspects of physical functioning, vitality and general health dimensions than did the non-MS control population. In addition, although there was a correlation between EDSS and QOL, the correlation was lower than expected (Pittock et al., 2004).

I.1.3.5.1) Types

Examining health related quality of life might be more relevant than general quality of life. HQOL refers to an individual's assessment of the impact of their health problem and its treatment on their ability to perform activities and their social/family/work roles (Fischer et al., 1999).

I.1.3.5.2) Prevalence

A population-based study found that PwMS had lower scores on the general health dimensions of the SF-36 QOL measure compared with the general US population. However, many other domains including pain, emotional role, mental health, and social functioning were similar between MS and non-MS populations (Pittock et al., 2004). These similarities in pain likely were due to the way in which the questions were asked as it has been shown that the instrument has a strong impact on the type of data generated (Schwarz, 1999) Also, although rates of pain in general were not different between MS patients and the general population in the Schwarz study, type, persistence and emotional correlates may be different. Additionally, there are issues to consider when using this measure with significantly disabled MS patients due to ceiling and floor effects (Hobart et al., 2001).

Health quality of life for PwMS in different domains for different groups, depends on severity, duration and clinical course (Benito-Leon et al., 2002) and may be moderated by emotional adjustment (Benito-Leon et al., 2003).

I.1.3.5.3) Assessment

In assessing quality of life, it is important to determine which factors to assess for that specific population (Lintern et al., 2001). Assessment of quality of life within MS, particularly for those with more significant disability, must be specifically tailored to that population as many generic quality of life scales rely heavily on physical measures and may not represent the way individuals evaluate their quality of life (Lintern et al., 2001).

Many measures may be used to assess quality of life for PwMS including: the Functional Assessment of Multiple Sclerosis (FAMS), the MSQOL-54, the Disability and Impact profile, the Hamburg QOL questionnaire in MS, the Leeds MSQOL, the MSIS, the MSQOL Inventory, the RAYS, The Pfennings HRQoL Instrument, QOL-Index MS–version, and performance scales (Benito-Leon et al., 2003).

I.1.3.5.4) Etiology

A poorer quality of life has not always been found to be correlated with increasing disability. Quality of life may be more significantly impacted by recent diagnosis (Ford et al., 2001). Also, other factors such as cognitive impairment may have a significant impact (Benito-Leon et al., 2002) although this has not always been supported (McIntosh-Michaelis et al., 1991). Emotional adjustment to illness and subjective disability have also been shown to be significantly correlated with health-related quality of life (Benito-Leon et al., 2003). The relationship between quality of life and disability may be mediated by patient perceptions.

I.1.4) SUMMARY

All of the symptoms discussed in Section I.1 appear to interact. Unfortunately, comparably few studies have examined the impact of pain on the lives of MS patients, despite pain being a relatively common symptom. As a result, one of the major factors in patient experience may be overlooked. In Section I.2, the relationship between symptoms will be further examined and specifically with the link to emotional aspects of pain.

I.2) Psychological aspects of pain

In this section, pain and its psychological components will be discussed as the basis for the proposed research. In a recent review article 'Chronic Pain Secondary to Disability: A Review,' Ehde et al. concluded that assessment of the physical presence of pain in MS has been described and now researchers need to turn away from the evaluation of pain as only physical, to an assessment of the way in which this pain impacts on the person's psychological life, their social activities and their true level of disability (Ehde et al., 2003a). However, studies completed within MS patients are relatively few. Where possible MS work will be mentioned but there will also be extrapolation from other disease groups with pain.

Psychological factors, discovered in early studies, have subsequently been found to be influential in all types of pain. These factors will be discussed as a guide to important psychological influences that may play a role in overall pain experience.

Gamsa (1994a, 1994b) notes that pain is a complex, multifactorial phenomenon caused by the interaction of multiple physical and psychological causes that cannot be fully explained by organic causes. According to this theory, it may be the case that not all pain is caused by tissue damage and even when it is, sensory input does not always correlate with pain report (Gamsa, 1994b). The physical and psychological make up the dualistic theory of pain experience. Furthermore, the psychological aspects of pain may include attributions, expectations, beliefs, self-efficacy (the belief that one has the power to manage a situation), personal control, attention, problem solving, coping, self statements, pain behaviour and imagery. Therapies addressing any of these areas are all worth considering because any may assist in helping the person with pain.

Given the research on the psychological aspects of pain, theories regarding the purpose for the maintenance of chronic pain report and behaviour have been developed, e.g., maintenance may be due to the receipt of support from others based on portrayal of the sick role (Gamsa, 1994a). Gamsa (1994a) theorizes that emotionally-based pain can be displaced onto the body where it may be more bearable and easier to communicate to others and that for some

patients with chronic pain, this pain may relate to a physical manifestation of unresolved emotional conflict.

Studies of pain assessments between doctors and patients show that physicians often underestimate pain perceived by patients. Interestingly, this miscalculation is particularly true for more experienced doctors (Marquie et al., 2003). This may be due to the fact that scientific medicine has reduced the pain experience to the physical broadcasting of signals rather than to an interaction between the signals and the individual's interpretation of the meaning of those signals (Johansson et al., 1999).

The notion of pain as a tangible disease marker that can be communicated to others, may be especially true for MS patients, as many of the other symptoms that MS patients experience are invisible to others, such as fatigue, mood disorders, cognitive impairment, etc. Pain is a symptom that is socially acceptable to discuss and can be readily understood by others. Pain may be a physical manifestation of the understandable fear and anxiety. To an MS patient, pain may also be a signal (possibly an erroneous one) that they are getting worse, becoming more disabled or will be soon. The number of MS patients who reported pain as one of the most distressing symptoms increased with increasing age (Stenager et al., 1991). The psychological impact of pain is an issue in MS that needs to be addressed.

As described previously, in recent comprehensive studies looking at prevalence of pain in MS, point prevalence was found to be just about 50%. However, more than 50% of patients report symptoms that fit the definition of pain but less than 50% claim to have pain when directly asked (Rae-Grant et al., 1999). This implies that there is a sensation that fits an accepted definition of pain, but is not reported as pain by all of those who experience it.

Clinicians need to rely on clinical experience to find the best way to ask patients about pain. At this point, the most sensitive and appropriate way of questioning patients has not been established. Having more established guidelines may make the process easier for both the physician and patient.

Many previous pain prevalence studies did not include data on relevant patient characteristics, pain severity/duration and the psychological effect. Also, many early studies did not examine the impact of pain on the patient's daily life or

the emotional issues involved (Archibald et al., 1994). The following studies did attempt to measure these factors.

The Archibald et. al. study is one of the most relevant studies to the current study and will therefore be discussed in detail. Archibald et al. (1994) attempted to examine this problem using structured interviews that allowed the patient to comment on type of pain, severity, duration and interference with daily life. Headache was included along with other self-reported pain. Prevalence of pain was found to be 53%. The breakdown of pain prevalence by disease category was RR 54.4%, CP 52%, and B 100%. The difference between RR and CP was not statistically significant. Pain was not correlated with age or duration of symptoms. Disease duration and neurologic symptom severity were significantly correlated with number or pain hours per week but not with pain severity, number of sites of pain or pain related distress. Archibald et al. also looked at which regions of the body were affected by pain. The breakdown regions were as follows: leg 73.3%, arm 57.8%, head 53.3%, trunk region 48.9%. Seventy-six percent reported more than one region of pain and some patients reported more than one site within one region. In addressing the impact of pain on daily life, 57% of the participants who reported pain, stated that their ability to work had been reduced by half. Patients with pain had a reported worse mental health status than did the non-pain group. This illustrates the impact of pain on the mental health of patients. The authors suggest that MS patients should always be asked about their pain symptoms.

In summary, there have been a number of studies that have looked at different pain conditions associated with MS. Only a few have looked at pain and the associated issues as a general experience. The Archibald et al. study (1994) was one of the few that investigated pain in MS and the impact of pain on daily living.

In the current study, there was careful consideration made about which pain measures to use. There are many objective measures of pain available but these are really designed for more common or more acute types of pain. This study is particularly concerned about the subjective experience of pain in MS patients, because it may be the associated distress as well as the pain itself that contributes to disability in the broad sense of the term.

I.2.1) Mood related to pain

Pain and mood disorders tend to occur together, however it can be difficult to determine causality in the absence of prospective studies and it may be a bi-directional relationship (Clark et al., 2000). Clark et al. report that 60% of people with depression (non-MS) mention pain at the time of their depression diagnosis.

Magni et al. found pain and depression were interlinked, although pain predicted depression in a more powerful way than depression predicted pain (Magni et al., 1984). They suggest that depression may be secondary to pain in line with the theory that pain causes distress as a result of the limitations imposed on the patient's life and the disruption of normal life activities. Magni et al. note that the opposite situation, when pain follows depression, is less clear and they theorize that pain may be somatic manifestation of the psychological disorder. In fact, Holzberg et al. found that somatic components of depression were strongly linked to the physical impact of pain and that depression may be a more significant factor than reported pain level in the subjective evaluation of ability to function (Holzberg et al., 1996).

Anxiety also appears to be linked to pain. People with chronic pain (non-MS) have high rates of anxiety across the spectrum of manifestations of the disorder (Fishbain et al., 1986; Polatin et al., 1993). However, when lifetime prevalence rates are separated from current prevalence rates, lifetime prevalence rates for chronic pain groups are not that different from the general population but current prevalence rates are significantly higher in chronic pain groups (Dersh et al., 2002). Pain conditions may have the ability to cross over undetected into many areas of one's life.

Specifically within MS, the presence of co-morbid anxiety and depression rather than either one alone was correlated with patients reporting more somatic complaints, social difficulties and suicidal thoughts as well as poorer functioning (Feinstein et al., 1999).

Studies examining anxiety/depression and pain have shown an interactive effect. People with pain and depression have a higher degree of interference in daily activities (Ehde et al., 2003b). Treatment of Experimental Autoimmune Encephalomyelitis (EAE) with rats for behavioural symptoms of stress (marker for depression) was also successful at modifying their EAE symptoms (Stephan et

al., 2002). It may be that treating either pain or depression/anxiety can reduce the level of interference on daily activities leading to an overall better outcome. An outline of EAE is perhaps warranted here. EAE is an animal model of MS where myelin destruction in a specific genotype of mouse or rat causes paralysis of the hind limbs (Burkhardt and Kalden, 1997). Manipulations can be made to arrest or promote the detrimental immune cascade and affect the degree of disease in these animals. Although this model is certainly not a perfect one, it can provide some useful comparisons.

It has been demonstrated in the literature that experiencing chronic or acute pain can cause MS patients to have difficulty in their daily lives (work and family interactions) and create additional psychological issues (Archibald et al., 1994). Chronic pain has been shown to significantly reduce physical performance (Rudy et al., 2003). Self-efficacy expectations and perceived emotional and physical health have been shown to be predictors of physical performance (Rudy et al., 2003). As physical performance is strongly linked to psychosocial factors in disabled chronic pain patients, the reduction in physical ability may logically be also linked to depression.

Anxiety about pain will often exacerbate the pain sensation. In one study with healthy participants, it was shown that this phenomenon is linked to activity in the hippocampal network (Ploghaus et al., 2001). Ploghaus et al. used fMRI to examine the neural mechanism anxiety uses to cause increased pain. They produced a signal to 'warn' participants of impending pain, and then delivered the pain stimulus. Pain-related anxiety increased perceived pain intensity; modulating pain by manipulating anxiety level was associated with activation changes in the hippocampus.

Holzberg et al. (Holzberg et al., 1996) found that anxiety had a significant impact on self-reported psychosocial functioning in chronic pain patients although it did not impact their reported physical functioning. Eccleston et al. found that chronic pain patients had normal State-Trait Anxiety Inventory (STAI) scores that were well below those of people with clinical anxiety (Eccleston et al., 2001). They theorize that worrying about chronic pain is a normal process, which is specifically triggered by an increase in pain and specifically related to current distress. They suggest that the characteristic of worrying by chronic pain patients

does not arise from a general disposition to worry, or from a general disposition to anxiety.

Another group of researchers found that highly anxious individuals demonstrate hypervigilance both generally and specifically but this hypervigilance is also mediated by pain-related fear (Vlaeyen and Linton, 2000). Fear may lead to avoidance behaviour, which is one mechanism toward sustaining chronic pain disability (Vlaeyen et al., 1995). James and Hardardottir found that generally low anxiety people in a distraction condition were most able to tolerate pain whereas those who were generally more anxious did not respond as effectively to a distraction condition (James and Hardardottir, 2002).

It has also been demonstrated that people without pain but with pain-related fear are likely to develop new episodes of back pain (Vlaeyen and Linton, 2000). People with anxiety and pain tend to have increased sympathetic responses to pain and this drives attention toward that pain (Arntz et al., 1994).

Worry about pain also seems to affect level of disability. Health anxiety has been found to be a significant predictor of level of disability after controlling for pain severity (Hadjistavropoulos et al., 2004). Hadjistavropoulos et al. also report that health anxiety not only serves to increase disability and pain at one time point, but also continues to reinforce pain and disability over time.

Treatment for mood disorders will be discussed, as if these mood disorders related to pain are treatable, it would be possible to control for this factor. Interestingly, both depression and pain have been treated in the past using tricyclic antidepressants. However, dosage is specific for the indication, with pain being treated at far lower doses of these tricyclic antidepressants.

Alternatively, cognitive behavioural therapy has also been used with both issues independently and certainly could be used together. The strategy employed in this type of therapy is to use positive reinforcement to encourage the individual to monitor positive and negative thoughts, to recognise the connection between their mood, thoughts and behaviour, to be capable of examining the evidence against their irrational beliefs and negative thoughts and therefore to substitute more positive interpretations and to identify and change the irrational beliefs which produce a distortion of their experiences (Larcombe and Wilson, 1984).

Given that mood and fatigue appear to be linked, it is unsurprising that treating depression has a positive effect on fatigue as well (Mohr et al., 2003). This relationship may also be true for mood and pain.

If patients are expected to recall their pain accurately for historical or treatment evaluation, and pain is linked to changes in emotional state, then it is important to be aware of interactions between emotion and memory. There is evidence for emotion's effect on memory. A person's mood influences which aspects of the environment seem most relevant (Lewis and Critchley, 2003). Specifically, situations associated with more intense emotion are more likely to elicit a vivid memory. Moore and Oaksford (2002) found that verbal memory was not affected by emotional state in the short term but emotional state did affect the acquisition of a task over several days. They found that positive emotion led to better performance on a task involving visual memory but negative emotion did not enhance ability on a visual memory task (Moore and Oaksford, 2002).

When people have a mood disorder *and* a medical disease, their use of the medical care system is double that of someone without a mood disorder (Magni et al., 1994). Magni et al. found that these people suffer more psychological distress, generally have a poorer long-term outcome, and have a poorer self-assessment of their physical health including functional disability and more deterioration in social and work functioning. If these findings hold true within the MS population, people who have MS, a mood disorder (depression or anxiety), and pain, may have a particularly poor quality of life.

Restriction of emotions and negative affect have shown a poor prognosis for non-MS disease populations in terms of pain report. A theory to explain the relationship between emotional restriction and increased pain report is that with high emotional restraint there is a reduction in awareness of emotional reactions. In addition, the person attempts to change his/her emotions rather than accept them and this may lead to internal conflict. For example, high emotional restraint and negative affect have been shown to lessen survival time in a breast cancer population, another immune-mediated condition (Weihs et al., 2000). Therefore, high emotional restraint may be a particularly disadvantageous coping style. This may prove to be true within MS as well and the current study will examine this.

I.2.2) QOL related to pain

Studies of neuropathic pain, which include quality of life measures, have been primarily performed using patients with spinal cord injury. One study found that neuropathic pain severely affected patients' quality of life (Ahn et al., 2003). Neuropathic pain may be similar to some MS pain as it is characterised by sensations of 'burning, stabbing, pins and needles sensation or numbness' which matches some of the MS descriptions of pain (Ahn et al., 2003).

Quality of life has also been studied in amputees, which may offer a useful comparison group in terms of disability and pain. A study by van der Schans et al. looked at 437 patients with lower limb amputation (van der Schans et al., 2002). They report that amputees overall had a lower health-related quality of life (HQOL) than age matched controls for specific domains: physical function, role limitations due to physical problems, and pain. They note in this population, HQOL is impacted primarily by mobility and phantom pain; significant differences were found between amputees with phantom pain and those without phantom pain after correction was made for age, sex, level of amputation and bilateral amputation. Furthermore, the specific difference in HQOL in this population besides the domain 'pain' was in the domain 'role limitation due to emotional problems'. It is speculated that QOL for MS patients is determined largely by pain and emotional problems.

Aronson (1997) found that MS patients as a whole have a worse quality of life than an equally disabled group of non-MS people. At this time, it is unclear what role pain may play in this relationship (Aronson, 1997).

Most QOL measures include bodily pain as part of the assessment. Because these bodily pain questions are only a small portion of the assessment, it is possible to derive separate estimates for each factor included in the assessment. This will be further discussed in Section II.

All three types of pain described by Moulin et al. (Moulin et al., 1988), previously described in section I.1.3.1.1, are likely to be significant to patient quality of life and may impact on the individual's ability to work, rest and fulfil their role. In addition, untreated or unrecognised pain may also lead to depression, distress and anger.

Sherbourne et al. found that anxiety reduces quality of life in people with chronic medical disorders (non-MS) (Sherbourne et al., 1996). The relationship between anxiety and QOL also appears to be strong for MS patients. Janssens et al. found that anxiety and depression act as mediators in the relationship between disability status as measured by EDSS and QOL for MS patients specifically (Janssens et al., 2003b). After adjusting for anxiety and depression, Janssens et al. (Janssens et al., 2003b) found that EDSS was only linked to the physical aspects of QOL. Lobentanz et al. also found depressive mood as a main factor in overall QOL (Lobentanz et al., 2004). In summary, depression and anxiety appear to be the strongest predictors of a reduced quality of life in the MS population (Fruehwald et al., 2001).

Shawaryn et al. found that physical measures of MS effects, including ambulation, physical disease severity and memory function, predicted the physical aspects of health-related quality of life whereas information processing speed and efficiency predicted the emotional/mental aspects of HRQOL (Shawaryn et al., 2002). Since pain may contribute to physical and emotional disease severity, it will be interesting to examine pain's role in both physical and emotional aspects of health-related quality of life in MS patients.

Stress has an impact on disease states overall, particularly for those diseases which are immunoregulated, for example, in patients with cancer it has been found that patients with a higher overall distress score had a shorter time to recurrence of cancer following a remission (Levy et al., 1985) as well as shortened survival time (Gilbar, 1996). It is possible that emotional restraint in combination with stress decreases survival time, as previously mentioned. Specifically, it is the chronic distress associated with anxiety that has a more significant impact on health than anxiety caused by transient events. This relationship has also been found to be true for people with MS.

As the biological effects of MS can cause frank pain and as the issue of having a disabling disease can cause stress, it is important to understand the relationship between stress and pain in the MS population. Lack of clear biological models and an agreed-upon definition of stress have made examining the relationship between stress and MS symptoms and disease state difficult

(Goodin et al., 1999). The limited evidence for this relationship will be described in the following paragraphs.

Acute psychological stress has been shown to alter quantitative and functional aspects of immune function both for healthy controls and MS patients (Ackerman et al., 1996). Some studies have found differences in immune function following or during a stressful period (Ackerman et al., 1996, 1998).

The impact of stress, in general, has been shown to cause a range of negative health effects and in the MS population may contribute to brain lesions (Mohr et al., 2002). The relationship between stressful life events and disease exacerbation has been investigated since Charcot's time, with his observation that grief and changes in social standing may be related to the onset of MS (Mohr et al., 2002). The biological plausibility for the impact of stress on MS is that stress disturbs homeostasis and can alter the equilibrium of various hormones which impact on the immune system (Correa et al., 1998). Studies have not supported the link between stressful life events and MS onset although stress has been shown to be related to disease activity (Mohr et al., 2002).

Specifically, moderate life stressors may be related to disease activity; this relationship has received support from the EAE animal model. Chronic and varied moderate stress increases disease activity (Correa et al., 1998) whereas severe stress inhibits disease activity (Whitacre et al., 1998; Dowdell et al., 1999). Therefore, it is chronic low-level stress that is likely to be problematic.

Mohr et al. (2000) found support for the theory that psychological stress leads to worse long-term outcomes in MS. In their study, Mohr et al. found that increased conflict and disruption led to the development of Gd+ lesions eight weeks later (Mohr et al., 2000). As with the EAE model, this relationship was only seen between mild or moderate stressors (things that led to conflict and disruption of the daily routine) but not major stressors like death in the family.

Mohr et al. (2002) hypothesized coping moderates the relationship between brain lesions and stress so that a higher degree of emotion-based coping would lead to a stronger relationship between stress and new brain lesions. This hypothesis was somewhat supported in their study, however the study design limited the results (Mohr et al., 2002).

Mohr et al. in their meta-analysis, found a significant association between stressful life events and exacerbation in MS (Mohr et al., 2004). They state that although the effect size is modest, it is clinically meaningful and suggest that management of the factors leading to stress for the individual may help to alleviate the immunologic changes leading to increased risk of exacerbation. It seems logical that stress plays an important role in clinical exacerbations. However, possibly due to the complexity of assessment of stress, this has not been empirically supported.

Illness perceptions (one's subjective assessment of illness) may be one of the most important variables in determining quality of life. In one study, illness perceptions were the most important variables in determining the variance in psoriasis patient outcomes possibly due to pathological worry but not to coping styles (Fortune et al., 2002). Fortune et al. found that patients who used avoidance and emotion-focused coping had significantly higher anxiety and disability scores. Higher anxiety scores were not enough to explain the overall lower QOL in psoriasis patients. The results could only be explained by illness perceptions overall. Therefore, coping styles may explain level of anxiety and or depression but perhaps only illness perception can explain the variance in QOL.

Illness intrusiveness is a concept which has been studied in people with MS and relates directly to QOL with respect to pain as well as fatigue, mood disorders, etc. (Shawaryn et al., 2002). Illness intrusiveness is the degree to which an illness permeates one's overall thought processes and self-identity. Shawaryn et al. believe that illness intrusiveness acts as a mediator between the physical and cognitive aspects of MS and the health-related quality of life. They looked at the impact of illness intrusiveness on fatigue. After controlling for illness intrusiveness, the impact of physical variables on health-related quality of life was much less significant. Mobility limitations, as well as learning and memory deficits, contributed to fatigue if illness intrusiveness was high.

Jopson and Moss-Morris investigated whether illness representations impacted on adjustment to MS and found that illness representations did play a significant role in adjustment with affective and behavioural aspects of psychological adjustment playing a large part (Jopson and Moss-Morris, 2003).

Vaughan et al. looked at illness representations in an MS population and were interested in Leventhal et al.'s self-regulation model which proposes that people's illness representations are influential in determining their strategies for coping and emotional responses (Vaughan et al., 2003). According to Vaughan et al., the model consists of five components: identity (the social attachment to the illness), time-line (expected duration and course of the illness), consequences (short or long term effects of the illness), cause (factors leading to development of the illness), and cure/controllability (what the individual believes they or others can do to bring about recovery from the illness). The illness representations noted in their population were consistent with the medical nature of MS. These representations were linked to outcome, with those with high levels of depression having perceptions of a stronger illness identity, more serious consequences, acute time-line and low control. However, in contrast to the Leventhal model, Vaughan et al. believe these illness representations have effects on outcome not mediated by coping (Vaughan et al., 2003). It is difficult to discern whether coping was a mediating variable as this study and another have not examined coping in addition to illness representations (Jopson and Moss-Morris, 2003; Vaughan et al., 2003). It may be possible that illness representations are directly linked to coping styles.

Support for such a mediating variable comes from research on the impact of rehabilitation programs on MS patients (Patti et al., 2002). Patti et al. report that certain rehabilitation programs found a benefit to QOL but no benefit on impairment (as measured by EDSS). They note, improvement on the SF-36, may indicate a positive effect on functional disability. Even if certain mobility limitations cannot be improved, QOL can be improved and functional disability can be lessened (Patti et al., 2002). Another study by Freeman et al. found, following a rehabilitation program, that although there was no change on EDSS, there was improvement on the FIM (Freeman et al., 1997) and so functional disability was impacted and therefore QOL.

Such mediators highlight the importance of perception. One's physical symptoms do not directly lead to a lower HQOL; instead it is the assessment of those symptoms that may or may not lead to a reduced quality of life. In the current study, there was an attempt to determine some of those mediators. If

those mediators can be identified then treatment can include therapy targeted at changing those influences.

I.2.3) Coping related to pain

Types of coping strategies are important in dealing with disease impact not just in relation to pain. Specifically, it may be the mediating factor for the relationship between chronic distress and anxiety. This is also true for people with MS.

Coping strategies for chronic pain are often grouped into such categories as diverting attention, reinterpreting pain sensations, praying and/or hoping, and increasing behavioural activity.

Psychological coping is also important to disease overall. In general, problem-focused coping (behavioural attempts to modify, avoid, or minimize the threatening situation) is usually considered the most functional and most likely to alleviate physical and psychological distress (Ratsep et al., 2000). Alternatively, the authors note that emotion-focused coping (psychological attempts to moderate or eliminate unpleasant emotions) is related to poor outcomes and has been linked to psychopathology. Ratsep et al. believe coping styles are based on psychological and social factors and possibly on personality.

There are certain types of coping strategies that are considered functional and others that are considered dysfunctional. Strategies categorised as diverting attention and praying and hoping have been correlated with greater pain, disability, depression, pain related anxiety and poorer work status in chronic pain patients (McCracken and Eccleston, 2003). It has been shown in general that attempts to control uncontrollable situations can have a significant negative impact on adjustment to chronic health problems (Christensen et al., 1995).

Acceptance of pain is defined as a 'disengagement from struggling with pain, a realistic approach to pain and pain-related circumstances, and an engagement in positive everyday activities (McCracken and Eccleston, 2003). McCracken and Eccleston (2003) carried out a study to determine whether acceptance of chronic pain or coping with chronic pain leads to a better long-term outcome. They found that although coping variables were weakly related to acceptance of pain and pain adjustment, acceptance of chronic pain did lead to less pain, disability, depression and pain-related anxiety and better work status.

Acceptance of chronic pain may be more important for pain management than coping strategies. Acceptance of chronic pain is difficult to inculcate in a patient population. McCracken et al. propose that the way to accomplish this acceptance task is to shift the patient's focus away from unsuccessful attempts to control pain and towards participation in activities that the patient values leading to the pursuit of relevant goals (McCracken et al., 2004).

McCracken et al. attempted to determine whether different strategies pain patients used, led to more anxiety or depression. They found the biggest predictor of pain-related anxiety was non-acceptance of pain which they labelled dysfunctional coping (McCracken et al., 1999). Dysfunctional coping led to anxiety, regardless of pain intensity and depression status (McCracken et al., 1999). The dysfunctional coping group had more pain-related anxiety and were less likely to accept their pain (McCracken et al., 1999).

A study by Shaw et al. found that positive problem solving buffered the impact of low back pain severity on functional disability (Shaw et al., 2001). Positive problem solving skills were defined as optimistic, persistent, high self-efficacy, commitment to finding solutions and a high tolerance for frustration (Shaw et al., 2001). They found that impulsive and careless problem solving resulted in poorly-guided attempts to deal with pain, to frustration and an increasing feeling that the pain could not be controlled, which in turn resulted in a predicted steeper gradient of functional disability. Avoidant problem solving (inaction and reliance on others) also led to more functional disability but only after a recurrent pattern of symptoms. Shaw et al. suggest this approach may reduce emotional distress, but does not aid in maintaining physical functioning. In the Shaw study, problem solving was not linked to pain severity but more to individual personality characteristics. They believe it may be possible to alter these with intervention.

Bergstrom et al. found that there were three basic coping styles: adaptive, dysfunctional and interpersonally distressed copers (Bergstrom et al., 2001). They developed two intervention programs, one high intensity and one low intensity in order to determine whether there was an interaction between coping style and effectiveness of intervention. They did not find a difference in improvement by subgroup.

Interventions targeting coping styles and inappropriate cognitions relating to pain, have shown some success (Jensen et al., 2001). A group of 141 patients and their significant others participated in a 3 week, five and a half days per week, outpatient treatment program, aimed at improving pain-management skills and physical/psychological functioning based on cognitive-behavioural therapy and physical and occupational therapy techniques (Jensen et al., 2001). Participants completed pre- and post-outcome measures and were shown to have improved pain-related coping and cognitions and improved self-reported: physical disability, depressive symptoms and pain intensity. Jensen et al. and Coughlin et al. conclude that this type of intervention is capable of increasing the patients' self-efficacy for controlling their pain (Coughlin et al., 2000; Jensen et al., 2001).

Self-efficacy is another important factor in pain management. A study by Asghari and Nicholas (2001) examined the influence of pain management self-efficacy and pain behaviours. They found that confidence in the ability to perform despite pain was predictive of the resulting behaviour (Asghari and Nicholas, 2001). Having a sense of control over pain appears to be very significant to pain patients' health status.

Hopelessness may also be a factor in poor outcome. In a study by Everson et al. (1996), the risk of death due to myocardial infarction or cancer was increased with the degree of hopelessness expressed (Everson et al., 1996). Hopelessness itself, independent of depression or other risk factors, predicted adverse health outcomes. These findings may be corroborated by studies with MS patients.

Evers et al. (2001) examined both rheumatoid arthritis and MS patients, and found helplessness predicted both an increase in functional disability and the impact of the disease on daily life whereas acceptance predicted a decrease in disease activity, physical complaints and negative mood (Evers et al., 2001). Recognizing perceived benefits predicted an increase in positive mood.

In an attempt to determine the most effective non-pharmacological coping strategy for dealing with MS pain, studies have examined the use of attention and distraction methods. The literature on attention versus distraction-coping

strategies for the management of pain has been dominated by acute pain situations and most studies with chronic pain do not include MS pain patients.

For acute pain patients, distraction is a common strategy for pain management and this may be achieved through a number of routes. In a study of twenty-eight patients in a hospital for psychosomatic disorders, distraction significantly reduced the perceived intensity and unpleasantness of the stimuli at painful levels but not at non-painful levels (Lautenbacher et al., 1998). However, one large, multi-centre study was unable to find significant benefit from distraction even with the acute pain of IV insertion and venipuncture (Geissner, 1991; Carlson et al., 2000). In another study using electrical shock, no significant effect of either distraction or attention was found to influence pain sensation (Duker et al., 1999).

In the chronic pain condition, the efficacy of distraction for pain control is far less clear. In a recent study of burn patients during dressing changes, it was found that the sensory-focusing group reported greater pain relief compared to the music distraction group and a reduction in remembered pain compared to the standard practice group (Haythornthwaite et al., 2001). Haythornthwaite et al. also found that patients who catastrophized, i.e., had more negative thoughts focused on potential bad outcomes, had more pain, memory for pain and less satisfaction with pain control. This relationship is thought to occur through a model proposed by Leventhal and reported by Brownlee, Leventhal and Balaban (Brownlee et al., 1992). Brownlee et al. conducted a study to investigate whether individuals who focused on their symptoms and were frequent users of health-care providers exhibited stronger autonomic reactions when presented with health threats (Brownlee et al., 1992). The study was done using healthy undergraduates divided into three groups based on questionnaire responses. The group labelled 'hypervigilants' because they tended to interpret sensations as indicators of disease, showed a sustained increase and a slower return to baseline in cardiac responding when presented with verbal descriptions of threatening illness scenes. Interestingly, this group did not report more negative affect.

State trait anxiety may be an additional factor to consider. A study by Cameron et al. completed with women who were currently in remission with

breast cancer addresses this issue (Cameron et al., 1998). Their hypothesis was individuals with high trait anxiety would also have chronic activation of cognitive representations indicating illness. Trait anxiety was defined as 'individual differences in the tendency to view the world as threatening or dangerous.' Those with more trait anxiety had greater sensitivity to tamoxifen-induced symptoms, an increase in attribution of symptoms to health threats, an enhanced worry about disease, and a stronger impulse to engage in protective behaviour.

The relationship between attention and distraction within perceived pain may play a role in coping mechanisms. The effect of a pain intervention is moderated by the amount of health anxiety each patient experiences (Hadjistavropoulos et al., 2000). Their study showed that health-anxious individuals' attention to sensations resulted in lower anxiety and pain than did distraction. Anxiety has been shown to be significantly correlated with pain related distress (Geissner, 1991; Visscher et al., 2001).

Studies have been conducted to attempt to identify how distraction might lead to a reduction in pain perception when presented with an induced pain. Bantick et al. found, using functional MRI with healthy participants in an induced pain situation, that painful stimuli take precedence over non-painful stimuli unless a concerted effort is made not to allow this to happen (Bantick et al., 2002). Reduced perception of painful stimuli also reduced activation of the pain areas of the brain: the insula, midcingulate and thalamus as well as brain areas relating to attention for cognitive tasks including the perigenual cingulate and orbitofrontal regions.

Interest in the effects of distraction comes from the information-processing model of scarce attentional resources. Eccleston's model proposes that attention for pain competes with the nociceptive input, denies the allocation of necessary resources since both information sources are equally likely to need resources (Eccleston, 1995b). This means that pain may impair an individual's ability to use a coping strategy. Eccleston reports this relationship has been demonstrated for experimental pain when participants are given a distraction task resulting in the level of reported pain decreasing but the performance on the task being impaired. In another study, Eccleston found that chronic-pain patients with high-intensity pain showed impaired performance on an attentionally demanding task when

compared to low intensity chronic pain patients and normal controls (Eccleston, 1995a). Even the low pain patients were not coping with the pain while they were engaging in the attentionally demanding task. They were instead switching back and forth between the two activities.

As MS patients have been shown to exhibit a high degree of clinically-significant anxiety (Feinstein et al., 1999), it is reasonable to examine the effect of attention versus distraction on reducing pain as this type of comparison has not been done in this population. Examination of the impact of attention or distraction on perceived pain is warranted, as the objective is to decrease both anxiety and pain.

Catastrophising also is an important factor in determining success in pain management. Catastrophising is defined as exaggerating the negative consequences of a situation. Catastrophising cognitions are ones in which symptoms produce negative thoughts that are focused on potential negative outcomes of the pain and underlying disease states. This type of thinking predicts higher levels of pain, memory of pain and satisfaction with pain control (Haythornthwaite et al., 2001).

People who have been found to catastrophise in response to pain, also have higher pain intensity, emotional distress and functional disability (Giardino et al., 2003). Giardino et al. argue that catastrophising may act as a coping style for obtaining social support or assistance. They found that more of the people who catastrophise, in response to sensory rather than affective pain, are living with a spouse or partner. Also, those who use catastrophising to cope, engage in more solicitousness in their relationships. Giardino et al. found evidence for a significant moderating effect of perceived solicitous responses to pain behaviour for affective rather than sensory pain.

However, others believe that catastrophising is separate from coping strategies and shows a much stronger correlation with pain-related anxiety (McCracken and Eccleston, 2003). Health-anxious individuals report more catastrophising, seek more reassurance and are less able to engage in protective strategies (Vlaeyen and Linton, 2000). Other studies show that pain catastrophising was a better predictor of pain-related fear than physical signs and

pain severity (Vlaeyen et al., 1995) and a strong predictor of chronicity of pain (Burton et al., 1995).

Crombez et al. report that pain patients with catastrophic thinking presumably remain attentionally fixed on threatening information for longer than non-pain patients or non-catastrophising patients (Crombez et al., 1999a). A study by Van Damme et al. looked at length of time to disengage from a pain cue when the cue was not followed by a painful stimulus; people who were high in catastrophising showed an added latency in disengagement from this pain cue (Van Damme et al., 2002). Peters et al. found that a longer pain duration predicted increased catastrophising in a general chronic pain population (Peters et al., 2005).

Evidence for the malleability of pain cognitions comes from experimental research. Rode et al. required both participants with pain and without pain, to take part in a squeezing task as well as in a distracting task (Rode et al., 2001). Subgroups of the patient and normal control groups were given one of three sets of instructions. One group was told the task was a 'muscle stamina and strength task;' another was told it was a 'pain tolerance task;' and the third was told 'the next task is a squeezing task.' The pain and non-pain groups were asked to rate the level of discomfort immediately after the task, and, at the completion of the tasks, to rate the average and maximum pain experienced during squeezing alone and in combination with the distracting task. All participants who were told it was a pain tolerance task, rated the task as much more painful in retrospect although there was no difference across the groups immediately after the task. This result supported the use of cognitive therapy in helping the individual both to identify and alter coping strategies in response to pain (Morley et al., 1999).

Results of studies with non-MS chronic disease populations, suggest that people can adopt a certain role based on the situation they are placed in. Extrapolated to the MS population, this means some people after being diagnosed with MS, may adopt a certain idea about their lack of control, and consequently be unable to cope in a problem-solving way.

This theory of self-induced dependence has been explored (Langer and Benevento, 1978). Langer and Benevento theorized that learned helplessness occurs when a person with prior experience with aversive outcomes comes to

interpret the response to the event and the outcome of the event as independent entities; instead of interpreting them as somewhat linked. By interpreting the events as independent, the person may decide not to attempt to alter the outcome as it is seen as futile. Langer and Benevento demonstrated that it was not necessary to fail at a task to develop self-induced dependence or learned helplessness. Placing labels on people may create self-induced dependence. This finding may have implications for some people with MS.

McCracken (1998) found that acceptance of pain is helpful for pain management by reducing distress and level of disability (McCracken, 1998). This finding does not conflict with Langer and Benevento's findings. Rather, it compliments the idea that labelling leads to distress. It is the acceptance of pain, but not the acceptance of the predestined effects of pain (i.e., disability, fear about pain) that may be most important. Acceptance of pain allows a problem-focused approach to pain rather than emotion-based coping. McCracken (McCracken, 1998) suggests that it is important to address the pain, as it is, accept it, and move on to other issues in life.

The successful coping strategies for people with MS may be different to the successful strategies for people without MS. In examining coping styles for disease related stressors, Ratsep et al. found that neither extraversion nor openness to experience were associated with task-oriented coping; agreeableness was associated with avoidance coping strategies (Ratsep et al., 2000). There was a positive correlation between neuroticism and emotion-focused coping and this relationship was even stronger than that for normal controls. Disease duration and severity were not related to coping styles. There may be an important distinction between adaptive coping styles for dealing with MS-related distress rather than ordinary stressors, or dealing with controllable versus non-controllable stressors (Folkman and Lazarus, 1980).

Strategies for coping with chronic disease have been studied with patients with MS as well as with patients with other chronic diseases. An instrument designed to elucidate illness cognitions as a mediator between stress and illness is the 'Illness Cognition Questionnaire' which has been specifically validated using an MS population (Evers et al., 2001). The questionnaire addresses the constructs of helplessness, acceptance and perceived benefits. Evers et al.

suggest constructs related to the concept of control (i.e., helplessness, hopelessness, cognitive distortion) have been found to predict long-term unfavourable outcomes, and it may be important in this population, who are exposed to this long-term stressor (MS), to be aware of any maladaptive thinking.

A study by Devins et al. (1993), compared the degree to which illness intrusion occurred in MS patients versus patients with end stage renal disease or rheumatoid arthritis (Devins et al., 1993). They found MS was significantly more intrusive into lifestyles, activities and interests than for the other two groups. Elevated intrusiveness for MS was found in terms of work, active and passive recreation, self-and religious expression, financial situation, family, marital and sex life as well as other social relations.

Pakenham recognised the lack of research on coping and specific illness stressors in MS (Pakenham, 1997). Pakenham did a study of MS patients and their caregivers using interviews and self-administered questionnaires that addressed all problems related to MS. Participants were also asked to identify their 'main MS-related problem'. He found support for the use of the stress and coping model of adaptation to MS and that the more their MS-related problems were assessed as threatening, the more likely the patient was to report higher levels of depression, global distress and poorer social adjustment. It was not merely the assessment of threat due to the main-MS problem that determined adjustment success but rather the conglomerate of the different MS problems.

A follow-up study by Pakenham specifically tested a stress and coping model and its impact on adjustment to MS (Pakenham, 1999). In this study, Pakenham found that emotion-based coping led to poorer adjustment whereas problem–focused coping was associated with better subjective health status.

In a later study by Pakenham (Pakenham, 2001), a new measure was developed specifically to assess coping in MS patients; previously, the available measure was the Ways of Coping Checklist (WCC) (Folkman and Lazarus, 1980). This new Pakenham measure is called the Coping with MS Scale (CMSS). In this measure, there are seven factors: problem solving, physical assistance, acceptance, avoidance, personal health control, energy conservation, and emotional release. An advantage of the CMSS over the WCC is that it asks about physical assistance.

The CMSS uses the statement "How often have you tried each of the coping strategies in dealing with your main MS-related problem?" (Pakenham, 2001). Pakenham looked at direct problem-solving strategies or more emotional 'problem-solving' solutions.

In studies using this measure, passive avoidance with emotion-based coping was correlated with poorer adjustment; problem-based coping was correlated with better adjustment. The CMSS assessment may result in over-attribution of problems to MS. Other negative health effects that occur in normal living may be disproportionately attributed to MS, whether or not this is truly the case.

It may appear that the previously cited authors had different ideas of what made successful and adaptive copers. The authors used different terms for their successful copers and unsuccessful copers however, it seems they were largely in agreement. Those individuals who did not accept pain, ruminated on their pain, felt hopeless, had low self-efficacy, catastrophized, had a lot of illness intrusion and blamed others, do not do well, both in terms of pain and QOL.

I.2.4) Cognition related to pain

There are several factors that can affect the way we process all information including pain. Examination of the impact of these factors is a main interest in the current study. Pain monitoring appears to be primarily controlled in the frontal lobe (where monitoring of the external world occurs), and plausibly competes for resources with short-term memory tasks and consequently impairs task performance (Lorenz et al., 2003). Experimentally, pain has been shown to lead to difficulties with concentration and memory (Crombez et al., 1999b). When a new stimulus is introduced, the ongoing activity is suspended while attention is drawn to the new item (Eccleston and Crombez, 1999). Duration of suspension is dependent upon several factors such as pain intensity. However, this relationship appears to be mediated by the threat value of chronic pain (Crombez et al., 1999b).

Pain-related fear is one of these factors. Pain-related fear is responsible for the development and maintenance of general distress and lowered ability to accomplish tasks of daily living (Crombez et al., 1999a). The strongest correlations were for pain-related fear and measures of self-reported disability

and behavioural performance (Crombez et al., 1999a), rather than with pain intensity or any other subjective pain assessment. Threat assessment has been shown to be the critical factor for pain-related fear. If a participant knows when a noxious substance will be administered, interference with the current task is reduced (Eccleston and Crombez, 1999). In addition, if pain is not the predominant threat, it has virtually no interference with the current task and may even lessen the pain sensation. Pain may even be assessed as less severe than controls will in a neutral setting. If pain is the predominant threat, the pain group will assess equivalent pain as more severe than controls will in a neutral scenario.

An example of pain-related fear influencing the experience of pain can be most profoundly shown by a study using arachnophobics (Janssen and Arntz, 1996). In this study, the arachnophobics rated pain as less severe when presented with a spider while being given electrical stimulation. The authors theorize this result was due to diverted attention (towards the spider) leading to reduced anxiety regarding the non-attended stimulus from the electrical stimulation.

Body schema may be another of these factors. Pain can affect the way in which one views the physical characteristics of one's body, i.e., one's body schema. A study by Schwoebel et al. showed that patients with chronic unilateral arm pain had slower response times when asked to identify the position of a limb in a picture made when the limb was the same one as their affected limb (Schwoebel et al., 2001). This study did not require any movement of the affected limb but may have triggered imagined movement (Schwoebel et al., 2001). This illustrates the way physical pain can cross over into psychological body schema.

There have been many studies on the cognition and pain relationship. Possibly one of the most classic measures used for to study this is the Stroop test of attention. In this test, the subject is presented with one colour name in another ink colour (red, blue, green) and the participant is asked to name the colour of the ink rather than the word spelled (Stroop, 1935). Latency in naming is due to distraction from the target stimuli. Theoretically, the more the alternative

task is distracting, the longer the latency period. These tasks have been modified by using different distracters to address different populations.

The modified Stroop is given with emotionally relevant words presented in different colours. The participant is asked to name the colour of the word, rather than saying the word. In tasks using the modified Stroop method, the theory is that when anxiety-relevant words are presented, they have an emotional meaning to the participant. As attention is drawn to those words, the participant takes longer to say the colour (Roelofs et al., 2002).

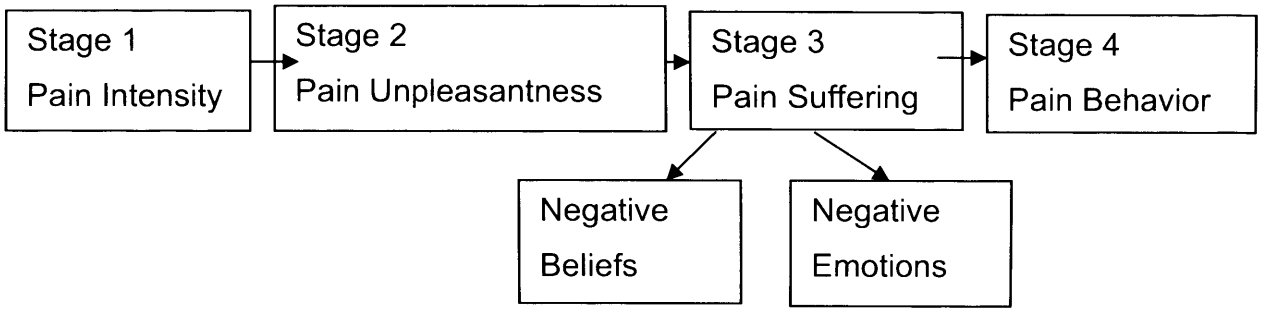
The relationship between pain and cognition is another important issue for the current study. Pain has been shown to impair cognitive function. This relationship is especially true for more attention-demanding tasks. This result may be due to attention being diverted towards the pain (Park et al., 2001). However, when emotional distress is controlled for, this relationship disappears (Kewman et al., 1991). Depression has been found to mediate the relationship between pain and cognitive abilities. When depression was controlled, effects of pain on cognition were no longer significant (Brown et al., 2002), a finding consistent with results from other studies, that the psychological distress resulting from pain diverts the attention, rather than the pain itself diverting the attention (Kewman et al., 1991; Brown et al., 2002).

All of the following have been shown to alter pain perception: attention, emotional state, expectation, and changes in consciousness. These are believed to alter both pain perception and pain transmission in the forebrains of humans. Attending to another sensory experience leads to parallel reductions in unpleasantness and intensity of pain (Villemure and Bushnell, 2002).

Wade and Hart (2002) created a model to examine the relationships between the four stages of pain processing and attention among chronic pain patients. In their model, the stages are:

FIGURE I.2.3.1

FOUR-STAGE MODEL OF PAIN PROCESSING (WADE AND HART, 2002)



Using this preliminary model with their study, they found that attentional impairment was only associated with suffering and illness behaviour and not with pain intensity. Their interpretation of the findings is that the same brain regions mediate attention and process emotional and evaluative components of the pain experience. A greater degree of pain-related suffering limits the supply of neural structures for attentional control.

Pain-related fear, body schema, and the relationship between pain and cognition are all areas that are relevant to the current study. All of these areas may contribute to pain related distress.

I.2.4.1) Cognitive bias

One main focus of the current study is the examination of cognitive bias in MS. Cognitive bias is a term used to describe an attentional bias toward specific types of material. The origins of this interest in cognitive bias, comes from anxiety studies looking at anxiety and bias toward material that is anxiety provoking. The concept behind this research is that irrational thoughts and dysfunctional beliefs play an essential role in the maintenance and origins of anxiety (Musa and Lepine, 2000). Cognitive bias is an important area for the current study. In preparation for the examination of cognitive bias in the current study, a review of the literature follows.

Watkins et al. refer to mood-congruent memory (MCM) as the ability to recall information better which is congruent with one's mood (Watkins et al., 1992). They expected a recall advantage for items learned in one mood state and recalled while in the same mood state. Watkins et al. report that this MCM may contribute to the maintenance of depression. In general, memories that are more highly processed (more associations made between other memories, etc.) are easier to retrieve.

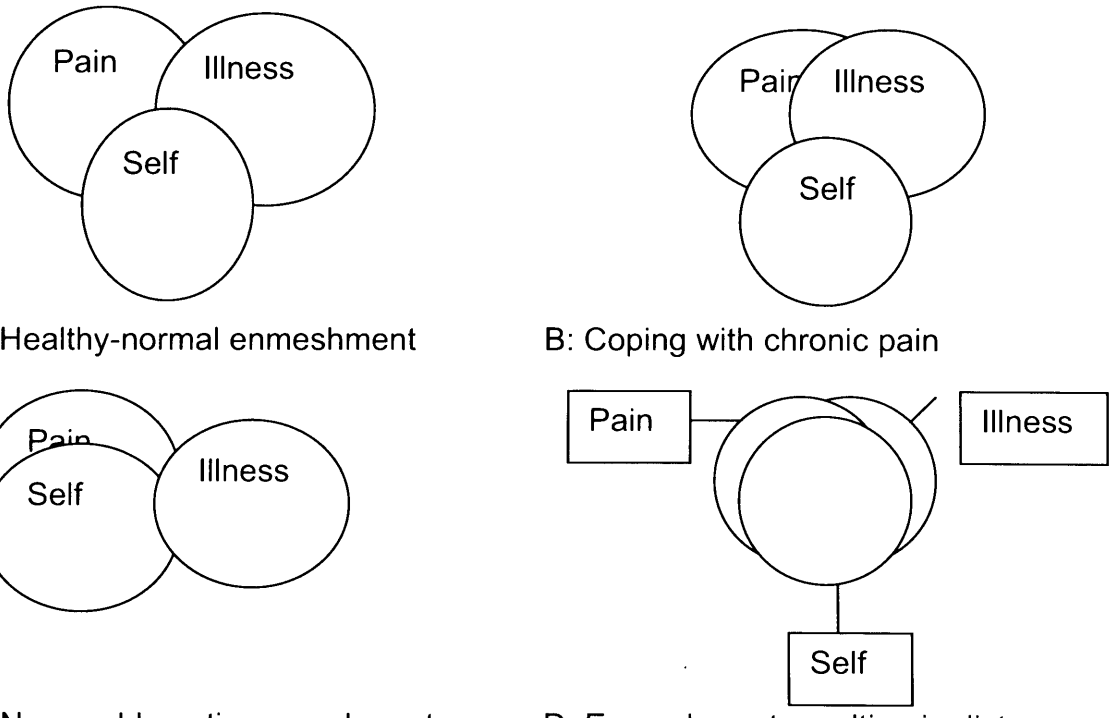
In a study of socially anxious and non-anxious individuals who read a passage and had to remember it, there was no difference in memory for the details contained in the passage for the two groups (Brendle and Wenzel, 2004). However, they did differ in the positive and negative interpretations of the details in the passages. Specifically, the socially anxious participants made fewer positive and more negative interpretations, particularly for the passages that were self-relevant.

Pearce et al. studied mood congruity in chronic pain patients and controls using both immediate and delayed recall (Pearce et al., 1990). Generally, pain patients recalled more pain related words than did the non-pain controls. Non-pain controls recalled more words total (Pearce et al., 1990). Pearce et al. did an additional experiment with induced pain with healthy volunteers. They did not find an effect of mood congruity in this experiment and hypothesize that it was the status of being a pain patient rather than the state of being in pain that causes the effect. The emotional experience for experimentally induced pain and naturally occurring pain may not be identical and perhaps this difference is a critical factor.

In their review, Pincus and Morley (2001) conclude that it is the interaction of pain, illness and self-concept that leads to an information processing bias. The following model explains their view of the relationship between cognition, affect and chronic pain:

FIGURE I.2.3.2

OVERLAP OF PAIN, ILLNESS AND SELF-SCHEMAS (PINCUS AND MORLEY, 2001)



A: Healthy-normal enmeshment

B: Coping with chronic pain

C: Non-problematic enmeshment

D: Enmeshment resulting in distress

The degree of overlap of all three, and perhaps the overlap of each of the corresponding two pairs as well, may represent the degree of information processing bias.

The effect of depression on memory is important to consider when looking at any studies using cognitive measures. Denny and Hunt (1992) found depressed participants recalled more negative words than positive words; non-depressed participants did the opposite. When using word fragment completion, which measures implicit memory rather than explicit memory, they found the difference between positive and negative valenced words disappeared. Denny and Hunt argue that when using a free-recall task, negative information receives preferentially deep encoding that makes the information more easily accessible. Depressed individuals register positive events as well as negative ones, but are less likely to be able to recall the positive ones (Denny and Hunt, 1992).

In a study done by Elliott and Greene (1992), depressed patients showed a decrease in ability to recall words in both a free recall task and a cued-recall task (Elliott and Greene, 1992). Therefore, any evidence of depression must be taken into consideration when assessing results from studies on pain patients who may suffer from anxiety or depression.

Watkins et al. attempted to compare implicit and explicit MCM bias in depressed and non-depressed controls (Watkins et al., 1992). The implicit memory task was a word completion task and the explicit memory task was a cued-recall task. The authors found that controls actually had more intrusions of sad words than did depressed participants. They also found that MCM was exhibited for explicit memory but not implicit memory. Depressed participants recalled more depression related items but not more physical threat words. All in all, they conclude, it is more difficult to prime anxious people than either depressed people or controls.

Edwards at al. conducted a study with participants who had chronic pain with or without accompanying depression, and with depressed psychiatric patients without pain (Edwards et al., 1992). Participants were presented with a word list comprised of sensory and affective pain words and neutral (non-pain) words matched for syllables and frequency. They found that non-depressed, pain patients recalled more sensory than affective or neutral words. Depressed non-pain patients showed the same pattern as non-depressed pain patients. Depressed pain patients showed no significant difference between sensory, affective or neutral words although the trends indicated higher recall for both

types of pain words than for neutral words. Edwards et al. conclude that depressed patients without pain do not selectively attend to all negative material, but rather attend to specific types of negative material.

Pincus and Newman (2001) also conducted a study on recall bias and pain. Their study used cost to assess levels of health-care utilization and found that patients with the highest costs showed a recall bias for pain words (Pincus and Newman, 2001). They believe attentional bias is linked to pain and may mediate behaviour. One explanation is those with pain visit healthcare providers more, get more access to pharmaceuticals and tests, and spend more time thinking about and reacting to their pain. This area of cognitive bias will be explored more fully in the current study.

Any effect of anxiety on memory is also important to consider when looking at any studies using cognitive measures. The concept that people selectively attend to information with particular salience for themselves has been widely studied in patients with anxiety disorders. Studies have also investigated whether pain patients selectively attend to pain-related stimuli. Some of these studies have used memory as an indicator of attention and others have used attentional processing.

In a study by Asmundson et al. a dot probe task was used to examine attentional differences to pain and non-pain stimuli (Asmundson et al., 1997). There was no difference between pain and non-pain groups as a whole, however there was a difference if patients were divided by levels of pain-related anxiety. Not all pain patients were found to selectively attend to pain related stimuli but those people with pain-related anxiety did.

In a study of people with a current anxiety disorder, participants had to interpret sentences as either threatening or non-threatening (Eysenck et al., 1991). The currently anxious group was significantly more likely than either a recovered-anxiety group or healthy-control participants to choose the threatening meaning of the ambiguous sentence. The ambiguous sentences, particularly for the possible physical-threat meanings, were rated as significantly more unpleasant for the anxious patients than for the control participants.

It may also be important to consider any effect of fear of pain on memory when looking at any studies examining cognitive bias. Research has shown that

people who are fearful of pain report more negative experiences (McCracken et al., 1998). Pain states as well as fear of pain are capable of disrupting attentional processes and thereby worsening the experience of pain. The concept of 'fear of pain' is one way in which anxiety mediates the experience of pain. Pain affects information processing both in terms of attention (Eccleston et al., 1997) and memory (Pincus et al., 1993), however it is not known whether this is a cause or a consequence of chronic pain.

In order to better understand this relationship, Keogh et al, conducted a study on healthy people with a high fear of pain versus those with a low fear of pain (2001). They wanted to see whether there would be any difference in the participants' attention or memory for pain-related stimuli. They found a significant difference for the high-fear vs. low-fear groups in terms of a selective attentional bias specifically for pain-related material (Keogh et al., 2001). This implies that selective attentional processing is not simply a by-product of the chronic pain state but may be a pre-existing vulnerability. Depression alone did not affect cognitive bias towards pain-related stimuli.

Diagnostic status may also have an effect on memory. Wells et al. found that diagnostic status can influence the recall ability of patients depending on the type of material presented (Wells et al., 2003). Participants were asked to state whether adjectives described their pain or themselves as a whole (in terms of sensory, depression, illness, or neutral characteristics). They were then asked to recall the items in a surprise memory task. It was found that chronic pain patients showed a recall bias away from depression. Wells et al. theorized that being give a diagnosis might buffer chronic pain patients against depression-related material.

With all of the previously stated considerations in mind, it is also important to consider anything specific to MS patients when using this population for studies. Cognitive impairment is not thought to compromise the reliability and validity of self-report health measures, including the HADS (Gold et al., 2003). Therefore, self-report measures of the impact of pain should not be impacted by mild cognitive impairment. However, level of cognitive deficit has been shown to be linked to level of depression in the MS population (Shawaryn et al., 2002).

The influence of depression on memory (specifically within MS) is a consideration when assessing cognitive impairment. Depression has been shown to significantly impact memory, specifically within an MS population (Randolph et al., 2004). Arnett et al. found that depressed patients did significantly worse on reading span but not on word span (Arnett et al., 1999a). They determined that depressed MS patients showed a limited working memory capacity. Arnett et al. theorized that depression results in reduced attention capacity. When examining this relationship in another study, they found that memory capacity mediates performance specifically on timed tasks (Arnett et al., 1999b).

Additionally, It has been shown that people who focus excessively on bodily sensations and feel a lack of control over their environment may also experience more fatigue than those who do not do so and this may have an additional impact on cognitive testing scores (Vercoulen et al., 1996).

Cognitive bias is a central issue for the current study. Attempts will be made to assess whether bias exists and in which direction the bias is focused.

I.2.5) Models

Chronic pain has been associated with depression, anxiety and substance abuse. No one theoretical model has completely explained the causal relationship. It is important to note the strong relationship between pain and depression. A higher percentage of chronic pain patients than in the general population have first degree relatives with depressive disorders (Magni et al., 1984; Katon et al., 1985; Magni et al., 1987). Dersh et al. believe that the dominant model is a diathesis stress model with diatheses signifying pre-existing characteristics which are activated by the stress of the painful condition (Dersh et al., 2002). Fishbain et al. report five different major hypotheses proposed for the causal relationship between pain and depression: 1) antecedent hypothesis: chronic pain develops after depression 2) consequence hypothesis: depression follows chronic pain 3) scar hypothesis: episodic depression preceding pain which then predisposes individual to having depression after onset of pain 4) cognitive behavioural mediation hypothesis: the relationship between chronic pain and depression is mediated by cognitive variables 5) common pathogenic

mechanism hypothesis (Fishbain et al., 1997). Support for the scar hypothesis has been found in several studies.

The biopsychosocial model is a dynamic pain model that considers mechanical, physiological, psychological and social issues. This theory assumes that there is some type of pathology or change that generates the nociceptive input to the brain (Turk and Okifuji, 2002). This action is followed by perception or the interpretation of the input that is, in turn, followed by appraisal, or the meaning attributed to the pain. The appraisal phase also influences subsequent behaviours. Appraisals may be affected by a person's beliefs and social situation and can directly affect how one deals with the pain and shape the course of the future. Turk and Okifuji suggest one of the factors is patient belief regarding ability to control pain and interference of pain in activities of daily living. Along with these beliefs come issues regarding self-efficacy. An interfering variable is psychological functioning or mood state. This model has helped to develop cognitive-behavioural treatment approaches for chronic pain. In this model, it is critical to view each patient as an independent entity, rather than as a member of a homogeneous group, due to the specific levels of each factor working in combination for each person.

Turk and Okifuji also cite the reasons for failure of rehabilitation treatment: many patients refuse treatment; those that take part often drop out; and relapse rate is high. In addition, pain rehabilitation, even when it works, does not cure pain. Instead, it works by emphasizing self-control and self-management of symptoms. Patients who have been treated successfully with surgery or drugs still report a significant amount of pain. Chronic pain, as a chronic disease, is not 'curable' but manageable.

It has been said that the traditional biological models, which are designed to address acute pain issues, do not accurately describe chronic pain and it is necessary to determine how pain impacts on patient functioning (Benrud-Larson and Wegener, 2000). Leventhal and Everhart propose that once an individual has experienced a specific type of pain, a noxious stimulus will simply retrieve the memory of the previous pain and help to determine the emotional reaction (Izard, 1979). A multilevel processing model using both sensory and emotional mechanisms for response is needed.

A recent review article completed by Kearns et al, proposed that the biopsychosocial model of chronic pain also applies to MS (Kearns et al., 2002). This adapted model considers the experience of pain, associated disability and affective distress as variables in the experience of such pain.

I.3) Background to present study & hypotheses formation

This section will specifically address the origins of the development of the current study and the reasoning for the choices that were made regarding the measurements used.

The primary aim of the current research project was to develop a model of how emotional distress and chronic pain interact which will inform future clinical practice and facilitate more sensitive and appropriate questioning procedures and treatment of patients.

Development of this study stems largely from another clinical research study examining cannabis as a therapy for spasticity in MS (Zajicek et al., 2003). As a part of the psychological battery administered to a subset of subjects (two centres including the National Hospital for Neurology and Neurosurgery at Queen Square London) a pain measure was administered. This pain measure was the McGill Pain Questionnaire. In this sample of MS patients, a common response patients offered prior to starting the McGill was, "I do not really have any pain." Regardless, they were instructed to listen to the adjectives and identify any that pertained to them. Many who stated they had no pain, still chose many pain adjectives.

This created the first question: if they subjectively felt that they had no pain, what were these patients referring to with these adjectives? Was it pain or was it something else? Clinicians need to be able to ask patients about pain but the most sensitive and appropriate way of questioning patients has not been established. What would be the most effective way to elicit the most informative answers?

The second question: how would the psychological impact of these sensations be different if it was pain or if it was something else? These questions are derived from the argument that although pain is significantly linked to depression in most populations (Clark et al., 2000), anxiety may be more

significant in the MS population due to pain-related fear (Hadjistavropoulos et al., 2004). This is theorized to occur because as MS is so unpredictable (McDonald and Ron, 1999), pain may act as a signal that the individual is getting worse or having a relapse and perhaps pain may interact with a propensity toward mood disorders. If this is the case, this would be more true for SP than for PP (Vleugels et al., 1998; McDonald and Ron, 1999).

For the third question, the choice of name is proposed to have some link to anxiety/depression (distress) (Clark et al., 2000). This link may go in either direction, i.e., those with 'pain' may be more or less likely to be anxious than those who use the term 'discomfort.' This relationship is thought to work in one of two ways: people who use the term 'pain' may have more anxiety/depression due to having a higher intensity of pain (Magni et al., 1994). Pain is a more concrete concept whereas discomfort is a far less concrete concept. Therefore, people who use the term 'discomfort' may have more anxiety/depression due the difficulty in communicating their pain/discomfort to others in a way that others can fully appreciate, thereby not gaining their support (Holzberg et al., 1996). In addition, the naming as pain/discomfort may affect their coping style and pain attitudes and this description may impact their concept of their social support network and self-efficacy (Coughlin et al., 2000).

The fourth question is: as cognitive bias has been shown in other pain/chronic conditions (Pincus and Morley, 2001), cognitive bias may also exist in this population. However this cognitive bias may occur toward MS or pain-related stimuli or both (Watkins et al., 1992; Pincus and Morley, 2001). The type of bias will determine the factors involved.

Based on the previous literature and the questions outlined above, several hypotheses are proposed for this study.

I.3.1) McGILL ADJECTIVES & PAIN INTENSITY - HYPOTHESIS 1

Based on a clinical observation, that not all patients with appropriate pain symptoms report "pain" when directly questioned, this study will formally assess this observation and also determine how those MS patients reporting "pain" differ from those not reporting "pain" with respect to the intensity and qualitative aspects captured by the McGill.

Hypothesis 1.1

Not all patients with appropriate clinically apparent pain symptoms will report "pain" when directly questioned.

Hypothesis 1.2

Patients reporting "pain" when questioned will select a different pattern of adjectives from the McGill to describe qualitative aspects of their pain than those not reporting "pain."

I.3.2) MOOD RELATED TO PAIN - HYPOTHESIS 2

Pain is known to be linked to distress in many conditions. However, MS carries an increased risk of psychiatric morbidity with or without pain. Therefore, emotional distress links to pain in MS are likely to be complex.

Hypothesis 2.1

Patients reporting more pain will have higher anxiety and depression. Precisely, when the patient population is split based on pain intensity score, the groups will differ in their anxiety and depression.

Hypothesis 2.2

Patients reporting more pain will have more illness intrusiveness. Precisely when the patient population is split into high and low pain intensity groups, the groups will have significantly different pain attitudes and impact of MS

I.3.3) PAIN VS DISCOMFORT SUMMARY – HYPOTHESIS 3

First, in regard to pain report, it is expected that certain people with clinically apparent pain will term their experience pain. Others will have symptoms that might well be clinically apparent as pain but subjectively be termed discomfort by the patient.

Hypothesis 3.1

Those who report higher levels of pain will differ in their distress from those who report higher levels of discomfort.

Hypothesis 3.2

Those who report higher levels of pain will differ in the impact of illness intrusiveness from those who report higher levels of discomfort.

I.3.4) COGNITIVE BIAS SUMMARY - HYPOTHESIS 4

As cognitive bias has been shown in other pain/chronic conditions, the hypothesis is that cognitive bias may also exist in this population. However this cognitive bias may occur toward MS or pain related stimuli or both.

Hypothesis 4.1

Patients will exhibit a cognitive bias towards MS-related stimuli on a stem completion task. The bias will be mediated by anxiety and linked to coping style. Those patients employing an emotional coping style will show the most cognitive bias.

Hypothesis 4.2

Patients will exhibit a cognitive bias towards pain-related stimuli on a stem completion task. The bias will be mediated by anxiety and linked to coping style. Those patients employing an emotional coping style will show the most cognitive bias.

Hypothesis 4.3

Patients will exhibit a cognitive bias towards MS and illness-related stimuli on a recall task. The bias will be mediated by anxiety and linked to coping style. Those patients employing an emotional coping style will show the most cognitive bias.

Hypothesis 4.4

Patients will exhibit a cognitive bias towards sensory and affective pain-related stimuli on a recall task. The bias will be mediated by anxiety and linked to coping style. Those patients employing an emotional coping style will show the most cognitive bias.

Hypothesis 4.5

Patients will exhibit a cognitive bias towards pain-related stimuli in terms of speed to respond in a timed task.

Specific measures used to test these hypotheses and statistical analyses will be stated at the end of Section II.

II) METHODS

This study is comprised of four parts: The first is a pilot study. In this portion, the design and pilot of experimental tasks was completed. The second part was to gather a study sample and assess pain and distress for this sample using standard and new measures to characterise the population. The third portion was to complete experiments using newly designed cognitive processing bias methods. In the fourth portion, standard measures were used to characterise this MS group, in terms of disability, age, fatigue and other demographic variables.

In this chapter, Section II.1 will describe the pilot study; Section II.2 will describe the main study. Section II.3 will examine the data for the entire sample to illustrate the generalizability of the sample. In section II.4 there will be comparison across different measures for the entire sample to look for overlap between measures. All analyses in Section II address normality of the sample or appropriateness of measures and do not address the central hypotheses pf the study.

II.1) Pilot study

II.1.1) STUDY PARTICIPANTS

Ten patients were selected for the pilot study to complete questionnaires from the neurology department at Queen Square. A sample, which was as representative as possible of the Primary and Secondary MS population, was selected, paying particular attention to sex, age and socio-economic grouping.

Although this group was as heterogeneous as possible, patients would have been referred to a large tertiary neurological clinic in this public teaching hospital. Patients were selected for the interviews from MS patients known to the neurology departments at Queen Square. The study was approved by the Hospital's Ethics Committee and informed consent was obtained from all patients who agreed to participate in the study. Potential patients were approached directly while waiting for a scheduled appointment for another unrelated study. As this portion of the study was not a major time constraint, all ten people approached did consent to take part in the pilot phase.

The following was undertaken in order to address the four hypotheses described in Section I.3.

II.1.2) DESIGN AND PILOT OF EXPERIMENTAL TASKS

All techniques were standard procedures in health psychology.

The pilot study involved being given instructions, being asked to complete a diary for 5 minutes/day for two weeks to document their pain/symptoms and the weather for that day. At the same time as the patients were instructed on how to fill in the diaries, they were asked to list 5 or more words they associate with MS. These terms were later compiled and considered for use in the cognitive bias portion of the study. The instrument is shown in Appendix D.

The ten patients were instructed individually. Ten patients, 5 per group, were considered to be sufficient to show whether participants understand and are comfortable with the instructions. These patients were instructed to identify and describe their pain symptoms (attention group) or were instructed to focus on and describe the weather for that day (distraction group). Instructions required 10 minutes and each entry took approximately 5 minutes per day to record. They followed the instructions for one week and then were contacted by telephone and asked to switch to the other intervention for an additional week. Journals were returned using pre-addressed stamped envelopes. Journal entries were examined and analysed for content and length to ensure that both treatments required the same amount of focus and time to complete.

The pilot study, both in terms of the prompted 5 word list and free form diary entries provided many of the words that will be used for the cognitive bias measures in the main study.

Although the intention was to test the viability of using a diary as a part of an intervention, this process did not seem possible for the main study. However, issues identified during the diary exercise helped to select areas of study and measures for the main study.

A pool of terms likely to be associated with MS was generated by the literature search and the five terms listed by the pilot patients (at least nine months previously). The literature search covered journals, books and the Internet. The aim was to identify more words that patients might associate with MS. The McGill pain assessment and other pain assessments were used to

generate a pool of pain terms, both sensory and affective. A pool of neutral words was created from neutral words used for other cognitive bias assessments.

From these three pools, ninety-six words including words thought to be a) pain-sensory (physical sensation of pain) b) pain-emotional (emotional impact of pain) c) neutral (a word which does not fall into one of the three other categories) d) MS-related (words which you would specifically associate with MS) were presented to these pilot patients. They were asked to choose only one category for each word. As they were given 24 items that were expected to fall into each category, only four per category were needed for the Experimental Recall Learning Task (ERLT). For the stem completion task, items were taken from other cognitive bias measures (Edwards and Pearce, 1994) and added to with the words generated from the 5 words listed and checked using the 96 word category list.

This list was then administered to the pilot patients at a second timepoint. These patients were asked to sort the words for category. This pilot measure is shown in Appendix D. The same list of items was also ranked by MS medical staff for category. Words that were not unanimous or did not show an overwhelming majority for category were discarded. The remaining words were used for the cognitive bias measures. Results from both the pilot patients and staff rankings are given in Table II.1.2.

The word completion task was created mainly based on the Edwards and Pearce assessment (Edwards and Pearce, 1994). However, it was adapted to include MS leading stems. Also, one word was omitted from the sensory words as it did not seem as applicable to neuropathic pain (as is found in MS) and shooting was substituted for this word. Care was taken to avoid using the same words or lead of the same word in both the ERLT and Stem Completion Task. Additionally, words had to be of reasonable frequency in language to be included in the ERLT and with enough alternative choices with reasonable frequency for the Stem Completion Task.

TABLE II.1.2) PILOT PARTICIPANTS SEMANTIC RATINGS OF WORDS

	*	P1	P2	P3	P4	P5	P6	P7	P8	P9	P10	D	S1	S2	S3	S4
Pounding	**1**	**1**	**1**	**3**	**1**	**1**	**3**	**1**	**1**	**1**	**1**	**1:80**	**1**	**1**	**1**	**1**
Intense	2	1	2	1	1	3	1	1	1	1	4	1:70	1	1	1	1
Educated	**3**	**3**	**3**	**3**	**3**	**3**	**3**	**3**	**4**	**3**	**3**	**3:90**	**3**	**3**	**3**	**3**
Spasticity	4	4	4	4	4	4	4	4	1	4	4	4:90	4	4	1	4
Fatiguing	4	4	4	4	4	4	4	4	4	4	4	4:100	2	2	1	4
Selective	**3**	**3**	**3**	**3**	**3**	**3**	**3**	**3**	**4**	**3**	**4**	**3:90**	**3**	**3**	**3**	**3**
Fearful	2	2	4	4	2	4	2	2	2	2	4	2:60	2	2	3	2
Tingling	**1**	**4**	**1**	**4**	**1**	**1**	**1**	**1**	**1**	**1**	**1**	**1:80**	**1**	**1**	**1**	**1**
Tugging	1	3	4	3	2	3	2	3	1	2	3	3:50	2	1	1	1
Cruel	2	4	2	2	2	2	2	2	4	4	4	2:60	2	3	3	2
Promising	**3**	**2**	**3**	**3**	**3**	**3**	**3**	**3**	**2**	**3**	**3**	**3:80**	**3**	**3**	**3**	**3**
Tremor	**4**	**4**	**4**	**4**	**1**	**3**	**4**	**4**	**1**	**4**	**4**	**4:70**	**4**	**4**	**4**	**4**
Itchy	1	4	1	1	1	3	1	1	1	1	3	1:70	2	3	1	3
Vicious	2	4	4	3	3	3	1	3	2	1	4	3:50	3	2	3	2

1 = Sensory pain 2 = affective pain 3 = Neutral 4 = MS
D = determined majority NM = no majority

	*	P1	P2	P3	P4	P5	P6	P7	P8	P9	P10	D	S1	S2	S3	S4
Nimble	**3**	**4**	**3**	**3**	**3**	**3**	**3**	**3**	**2**	**3**	**3**	**3:80**	**3**	**3**	**3**	**3**
Numbing	4	4	4	4	1	3	4	4	1	4	4	4:70	2	1	1	1
Shaking	**4**	**4**	**4**	**1**	**4**	**4**	**1**	**4**	**4**	**4**	**4**	**4:80**	**4**	**4**	**4**	**4**
Informal	3	3	3	3	3	3	3	3	2	3	3	3:90	3	3	3	3
Terrifying	2	4	2	3	2	3	1	2	4	4	4	NM	2	2	3	2
Pinching	**1**	**4**	**1**	**1**	**2**	**1**	**1**	**1**	**1**	**1**	**1**	**1:70**	**1**	**1**	**1**	**1**
Splitting	**1**	**1**	**1**	**1**	**1**	**1**	**1**	**1**	**1**	**3**	**3**	**1:80**	**1**	**1**	**1**	**1**
Sickening	2	2	3	1	1	3	2	2	2	2	3	2:50	2	2	4	2
Protruding	3	3	3	3	3	3	3	3	4	3	3	3:90	3	3	3	3
Relapsing	**4**	**4**	**4**	**4**	**2**	**4**	**4**	**4**	**2**	**4**	**3**	**4:70**	**4**	**4**	**4**	**4**
Physiotherapy	4	4	4	4	3	4	4	4	4	4	4	4:90	3	4	3	4
Resounding	3	3	3	3	3	3	3	3	2	3	4	3:80	3	3	2	3
Punishing	**2**	**2**	**2**	**4**	**2**	**2**	**2**	**2**	**2**	**4**	**2**	**2: 80**	**2**	**2**	**2**	**2**
Throbbing	1	4	1	1	1	3	1	1	1	1	4	1:70	1	1	2	1
Prickling	1	4	1	4	1	4	1	1	4	1	3	1:50	1	1	2	1
Suffocating	**2**	**2**	**2**	**1**	**2**	**2**	**3**	**2**	**4**	**2**	**2**	**2:70**	**2**	**2**	**2**	**3**
Burning	1	4	4	1	1	1	1	1	1	1	4	1:70	1	1	1	1

	*	P1	P2	P3	P4	P5	P6	P7	P8	P9	P10	D	S1	S2	S3	S4
Wobbly	4	4	2	3	4	4	2	4	1	4	4	4:60	3	4	4	4
Stabbing	1	1	2	1	3	1	3	1	1	1	4	1:60	1	1	1	1
Tiring	2	4	4	4	4	4	2	4	4	4	4	4:90	2	2	4	4
Stony	3	2	3	3	3	3	3	3	2	3	3	3:80	3	3	3	3
Balance	4	4	4	4	4	4	4	4	4	4	4	4:100	4	4	4	4
Stiff	4	4	4	4	4	4	1	4	4	4	4	4:90	4	4	1	4
Flexible	3	4	3	4	3	4	3	3	1	4	3	3:50	3	3	1	3
Horrible	2	4	2	2	2	1	3	2	2	2	2	2:70	2	2	3	2
Boring	1	3	3	3	4	3	2	2	2	4	3	3:50	3	3	3	1
Searing	1	3	1	1	1	3	3	1	2	1	1	1:60	1	1	2	1
Annoying	**2**	**2**	**4**	**2**	**2**	**2**	**2**	**1**	**2**	**2**	**2**	**2:80**	**2**	**2**	**2**	**2**
Leaking	3	4	4	3	4	4	3	4	2	4	4	4:60	3	3	3	3
Uncoordinated	**4**	**4**	**4**	**4**	**4**	**4**	**4**	**4**	**4**	**4**	**4**	**4:100**	**4**	**4**	**4**	**4**
Dependence	4	4	4	4	2	4	2	2	2	4	4	4:60	2	4	4	4
Angular	3	4	3	3	3	3	3	3	3	3	3	3:90	3	3	3	3
Distressing	2	4	2	4	4	3	2	2	4	2	4	4:50	2	2	1	2
Crushing	1	4	2	3	3	3	3	1	4	2	3	3:50	2	1	2	1

	*	P1	P2	P3	P4	P5	P6	P7	P8	P9	P10	D	S1	S2	S3	S4
Shooting	1	4	4	1	3	1	1	1	1	1	1	1:70	1	1	1	1
Troublesome	2	4	2	4	4	3	1	2	4	4	4	4:60	2	2	3	3
Prime	**3**	**3**	**3**	**3**	**3**	**3**	**3**	**3**	**2**	**3**	**3**	**3:90**	**3**	**3**	**3**	**3**
Spasm	4	4	4	4	4	3	4	4	4	4	4	4:90	4	4	1	4
Wrenching	1	4	2	3	3	3	3	1	2	2	3	3:50	1	1	1	1
Discomforting	2	4	4	1	4	3	1	1	2	4	4	4:50	1	2	1	2
Imprecise	**3**	**4**	**4**	**3**	**3**	**3**	**3**	**3**	**3**	**3**	**4**	**3:70**	**3**	**3**	**3**	**3**
Rehabilitation	4	4	4	4	3	3	4	4	4	4	4	4:80	3	1	3	4
Cutting	1	1	3	3	1	4	3	1	1	1	3	1:50	1	3	3	1
Blinding	2	2	2	1	3	3	1	1	1	1	3	1:50	1	2	3	1
Spreading	3	4	4	3	1	4	3	3	4	4	3	4:50	3	1	3	3
Mobility	4	4	4	4	4	4	4	4	4	4	4	4:100	3	4	1	4
Weakness	4	4	4	4	4	3	4	4	4	4	4	4:90	4	4	1	4
Transient	3	3	3	3	3	3	2	3	4	3	4	3:80	3	1	3	3
Excruciating	2	4	1	1	1	3	1	1	4	1	3	1:60	1	2	1	2
Aching	1	4	4	4	1	3	2	1	1	1	3	1:40	1	1	2	1
Scalding	1	3	3	1	3	3	1	1	3	1	3	3:60	1	1	2	1

	*	P1	P2	P3	P4	P5	P6	P7	P8	P9	P10	D	S1	S2	S3	S4
Mild	2	3	3	3	2	3	3	3	4	1	3	3:70	3	1	1	3
Legal	**3**	**3**	**3**	**3**	**3**	**3**	**3**	**3**	**2**	**3**	**3**	**3:90**	**3**	**3**	**3**	**3**
Disability	4	4	4	4	4	4	4	4	4	4	4	4:100	4	4	4	4
Steadiness	4	4	4	3	4	4	2	3	4	4	3	4:60	3	4	4	4
Polished	**3**	**3**	**3**	**3**	**3**	**3**	**3**	**3**	**3**	**3**	**3**	**3:100**	**3**	**3**	**3**	**3**
Unbearable	2	4	2	1	1	3	1	2	1	1	4	1:50	1	2	2	2
Pressing	1	3	3	3	3	3	3	3	1	1	3	3:80	1	1	2	1
Tender	1	2	4	1	4	3	3	1	1	3	3	3:40	1	3	2	1
Gruelling	**2**	**2**	**2**	**1**	**2**	**2**	**2**	**2**	**2**	**2**	**3**	**2:80**	**2**	**2**	**2**	**2**
Amazing	3	3	3	3	3	3	3	3	3	4	3	3:90	3	3	3	3
Incontinence	4	4	4	4	4	4	2	4	2	4	4	4:80	4	4	4	4
Hoisting	4	4	4	4	4	3	3	3	3	4	4	4:60	4	4	3	4
Windswept	3	3	3	3	3	3	2	3	1	3	4	3:70	3	3	1	3
Miserable	2	4	2	2	2	3	2	2	2	2	4	2:70	2	2	2	2
Flashing	1	3	3	3	3	3	3	1	1	3	3	3:80	3	1	3	3
Beating	1	2	3	3	3	3	1	3	1	1	3	3:60	1	1	3	1
Killing	2	2	3	3	3	3	1	1	4	3	4	3:50	1	2	2	3

	*	P1	P2	P3	P4	P5	P6	P7	P8	P9	P10	D	S1	S2	S3	S4
Grand	3	2	3	3	3	3	3	3	3	3	3	3:90	3	3	3	3
Impotence	4	4	4	4	3	4	3	3	4	4	4	4:70	3	4	4	4
Collapsing	4	4	4	4	3	4	2	4	1	4	4	4:70	2	3	3	4
Youthful	3	3	3	3	3	3	3	3	4	3	3	3:90	3	3	3	3
Frightful	2	1	2	4	2	3	2	3	2	4	4	2:40	2	2	2	2
Heavy	1	1	4	4	2	4	4	4	1	4	4	4:70	3	1	2	3
Hurting	1	4	1	4	2	1	1	1	1	1	1	1:70	1	1	2	1
Wretched	2	4	2	2	2	3	2	2	4	2	4	2:60	1	2	2	3
Knotty	3	4	3	4	3	3	3	3	4	3	3	3:70	1	1	2	3
Treatments	4	4	4	4	4	4	3	4	4	4	4	4:90	4	4	3	4
Progressive	4	4	4	4	4	4	4	4	4	4	4	4:100	4	4	4	4
Swaying	3	4	4	3	3	4	3	4	4	4	4	4:70	3	3	3	3
Exhausting	2	4	4	4	4	4	2	4	4	4	4	4:90	2	2	4	2
Drilling	1	1	2	3	3	3	1	1	4	3	3	3:50	1	1	3	1

II.2) Main Study

In Sections II.2.2 through II.2.5, measures will be described in the order in which they were presented to the participants.

II.2.1) PARTICIPANT SELECTION

The consent to approach these patients was obtained from their own hospital consultants. It is not possible to be certain of how many people who were asked 'would you be interested in hearing more about a research study?' However, once they agreed to hear more about a research study, they were counted in the 115 people approached prior to visiting an outpatient clinic.

As pain was not a criterion for entry into the study, the expectation was for a sample with a wide range in pain experience (from no pain to severe pain). Of the 115, 102 patients were able and willing to complete the entire study and all results presented here reflect their responses. The 13 people, who did not complete the study, did not do so primarily due to time constraints. The 102 people were the only patients involved in the rest of the study. These participants only had to visit Queen Square for the initial battery of questionnaires.

Participants were invited to take part in an experiment on the effect of MS on their lives. It was not mentioned that the primary focus was pain so as to avoid introducing bias. Having obtained written consent, they first completed all of the cognitive bias tests and then went on to the questionnaire portion of the study. At the completion of the entire study, all participants were debriefed.

As motor impairment was overwhelmingly common in this specific study, the subjects were not asked to physically record any of their answers. Participants were given a book to follow along with the questions but all answers for all participants were recorded by the assessor [KH]. Additionally, as vision impairment can be a relatively common problem for MS patients, participants were not excluded based on vision difficulties. Given this, all questionnaires were read aloud to participants. While it is understood that the reading and recording of questionnaires may introduce bias due to unintentional nonverbal cues from the assessor, based on the participant population, these measures were necessary. If these mechanisms were not employed, participants would need to have been excluded. Also, with this method, all participants were treated equally rather than having different conditions for different groups of patients' impairment profiles.

The inclusion and exclusion criteria are described below.

Inclusion criteria:

1. Patients aged 18 years or over;
2. Clinically definite or laboratory supported MS.

Exclusion criteria

1. Current severe psychiatric disease (i.e. schizophrenia, psychosis);
1. Severe cognitive impairment such that patient was unable to give informed consent;
2. Recent exacerbation (within the last six months);
3. Recent change in immunomodulatory medication (within the last six weeks).

II.2.2) ASSESS DEGREE OF COGNITIVE-PROCESSING BIAS

Cognitive-processing bias is a well-known and accepted concept for researchers working with varied groups of chronic pain patients. The current methods to study this bias consist of tests that rely on complex memory and visual tasks, which are inappropriate demands for this progressive disease group. Therefore, some alternative assessments that relied less on memory and vision were designed to examine the same concepts. These tests included a stem completion task (Edwards and Pearce, 1994), an experimental recall task with a format similar to the California Verbal Learning Test (CVLT) but using pain words (Edwards et al., 1995), and MS words as well as an adapted Hayling sentence completion task (Burgess and Shallice, 1996) which tests the ability to end pain and non-pain related sentences with either congruent or non-congruent endings. In order to examine the degree to which participants exhibited evidence of having a pain cognitive-processing bias, the following three specially designed assessments were employed:

II.2.2.1) Stem Completion

A stem completion task was modified to include stems that can be chosen to be pain related. This task was designed and utilized by Edwards and Pearce (Edwards and Pearce, 1994). They used this task on health professionals, chronic pain patients, and controls. The task presents patients with 12 word stems (e.g., sha___, fea____) and participants are asked to write down the first

two words of any length that came to mind. All of the stems have at least one pain related completion and at least three non-pain related completions of greater than or equal frequency as the pain related completion (Carroll et al., 1971; Edwards and Pearce, 1994). Four words were chosen from the sensory and four from the affective categories of the McGill Pain Questionnaire and the remaining four are general illness terms. Added to this existing list were four stems that could be completed with an MS related word. The MS stems were chosen based on the pilot study findings.

II.2.2.2) Experimental Recall Learning Task

The ERLT was developed using MS and pain words. Participants were presented with a list of 20 words consisting of 4 leading/following neutral words, 4 sensory pain words, 4 affective pain words, 4 MS words, 4 neutral words. The pain words were taken from the McGill Pain Questionnaire, adapted for this type of assessment by Edwards, Pearce and Beard, (1995). The MS words were chosen based on a pilot study that involved asking patients to say the first five words they thought of in relation to MS. Format and instructions are identical to the CVLT. Before the list was read, participants were instructed:

i. (trial 1) You are going to hear a list of words. Listen carefully, and when I am through I want you to say back as many as you can. It doesn't matter what order you say them in – just say as many as you can. Are you ready?
ii. (trial 2) You are going to hear a repeat of the list of words. Again, I want you to say back as many as you can. Be sure to also say the words on the list that you told me the first time.
iii. (trial 3-5) I'm going to read the list of words. Again, I want you to say back as many of the words as you can, in any order, including words you may have already told me.

II.2.2.3) Hayling Sentence Completion Task

The Hayling sentence completion task (Burgess and Shallice, 1996) is a component of the Behavioural Assessment of Dysexecutive Syndrome (BADS) in which the beginning of a sentence is presented and the patient is required to complete a sentence in a sensible/non-sensible (congruous/incongruous) context. This task has been modified to use pain and non-pain sentence

starters. Error analysis is done for the non-sensible test. This error analysis is completed on the non-congruous endings with a Type A error being the more severe error and type B error being a more subtle error. To compute subtotal error scores for pain and non-pain statements, Type A errors are scored as 2 and Type B errors are scored as 1. Details of these measures are presented in Appendices E.

II.2.3) ASSESS ALL PAIN IN THE STUDY POPULATION

II.2.3.1) Semantic Differential

Participants were given a semantic differential (SD) measure to assess psychological wellbeing/distress (Walker and Sofaer, 1998) with an added portion to assess illness related factors. Semantic differential is based on Charles Osgood's system of connotation (Osgood, 1969). It is a plot of the semantic distance between two words. Participants are instructed to say how they feel 'most often these days.' In this case, participants are given two adjectives on either side of a five-point scale ranging from good to bad, for example.

This assessment was designed to determine the psychological distress of patients attending a pain clinic (Walker and Sofaer, 1998). This measure is designed to reflect the patients' perceived control over all aspects of life. The measure is shown in its current format in Appendix E. The SD consists of a 12-item, 5-point semantic differential scale which incorporates items taken from existing measures of depression (Beck et al., 1961), anxiety (Spielberger and Gorsuch, 1983), hostility and general well-being (McNair et al., 1982). Each item is scored as a 1 (positive) to 5 (negative) providing a total score of 12 (well-being) to 60 (distress). This specific tool was originally created to be a valid, brief, easily understood, acceptable and relevant measure to patients with chronic pain. It has been most widely used as a nursing measure but its basis in the above psychological measures supports its validity as a measure if psychological distress.

Factor analysis confirmed that the factor, distress, accounts for 53% of the variance. The coefficient based on a number of earlier studies, for the twelve items was 0.93. The test-retest correlation was 0.83 in a normal adult population that experienced no significant changes over the past week (Walker and Sofaer,

1998). These results indicate that this measure has a high level of internal and test-retest reliability.

The existing SD of wellbeing/distress will be termed the **Total Emotional SD**. The added portion with 5 illness related questions will be termed the **Total Disease SD**.

II.2.3.2) McGill Pain Questionnaire

Next the McGill Pain Questionnaire was administered (Melzack, 1975; Vermote et al., 1986). The McGill Pain Questionnaire (MPQ), which was created by Melzack, consists of seventy-eight pain adjectives. These adjectives are grouped into 20 groups. All terms fall into one of three categories: sensory, affective and evaluative. Some describe sensory experiences, some describe affective qualities, and others reflect degree of disruption due to pain. Participants are asked to indicate which word, if any, in a group best describes their pain. Scoring can be done by determining an overall score for the intensity of pain or it may be done simply by counting the number of items in each of the three categories. The MPQ has been found to be a reliable measure for current pain (Graham et al., 1980).

II.2.3.3) Pain Discomfort Scale

An adapted Pain Discomfort (PD) Scale was given next. In the adapted version, the original became the first part, the **Pain PD scale**, and the second part, the **Discomfort PD scale**, used the word discomfort to replace the word pain. The Pain Discomfort Scale (PDS) was designed to assess negative affect due to a patient's pain (Turk and Melzack, 1992). It consists of 10 items that the patient responds on a five-point Likert scale with zero being 'This is very untrue for me' to four being 'This is very true for me'. The data from the development of the scale indicate a high internal consistency and test-retest stability (Jensen et al., 1991). A factor analysis (Jensen et al., 1991) yielded four factors: pain intolerable, distress denial, denial of impact and emotional distress. The PDS was developed and validated for use with chronic pain patients. This is a strength for this study, as most pain assessments are primarily designed and validated for use with acute pain patients.

II.2.3.4) Survey of Pain Attitudes

Patients next completed the Survey of Pain Attitudes (SOPA) (Jensen and Karoly, 1991) to assess their beliefs about pain origin and possible treatment. This measure has seven subscales. The **Control** subscale is the extent to which participants believe they can control their pain. The **Disability** subscale is the extent to which participants believe they are disabled by their pain. The **Harm** subscale is the extent to which participants believe that pain means they are damaging themselves and also that they should avoid exercise. The **Emotion** subscale is the extent to which participants believe their emotions impact their experience of pain. The **Medication** subscale is the extent to which participants believe that medications are an appropriate treatment for chronic pain. The **Solicitude** subscale is the extent to which participants believe that others, especially family, should be solicitous in response to their pain. The **Medical Cure** subscale is the extent to which participants believe there is a medical cure for their pain problem.

II.2.4) STANDARD MEASURES USED TO CHARACTERISE THE MS GROUP

Using the following standard measures, of general intelligence and working memory, the population was characterised. The measures included the California Verbal Learning Test (CVLT) (Delis et al., 1987) and National Adult Reading Test (NART) (Nelson, 1982).

II.2.4.1) California Verbal Learning Task

The California Verbal Learning Task (CVLT) is able to quantify the ways in which participants learn or fail to learn verbal material. It is a brief assessment of strategies and processes employed by the participant to learn and remember verbal material. It measures the participant's ability to recall a list of 16 words (four words from each of four semantic categories) over five trials (Delis et al., 1988).

This test is given as five free recall trials. The maximum possible score for correct answers for any one of the trials is 16 and the maximum possible total score is 80. Total perseverations (the repeat of an already stated correct item) and total intrusions (stating an item which was not on the list given) are also computed. A semantic cluster score indicates listing two or more items from the

same semantic cluster in sequence. Each trial has a maximum possible semantic cluster score of 12; with five trials the total possible semantic cluster score is 60. Serial cluster score refers to listing 2 items or more in the order in which they were presented, has a total maximum of 15 per trial, and has a total score of 75. The primacy score, derived as the number of items recalled from the first four items given out of the total recalled, make up 25% of the possible events. The middle score (made up of the middle eight items) makes up 50%. The recency score (made up of the last four items listed) makes up 25% of the possible events.

II.2.4.2) National Adult Reading Test

The National Adult Reading Test (NART) (Nelson, 1982) was given next. It consists of words unlikely to be read correctly unless the person is familiar with them. It is composed of fifty words and each word is scored as correct or incorrect based on pronunciation. This test provides as estimate of premorbid IQ. It cannot be given to those with moderate to severe vision impairment, but as the font is large, most of those with mild vision impairment are able to use the test. The fact that those with profound vision impairment could not use the test, explains why there is an N of 98 on all reports regarding the NART score, as 4 participants were unable to take the NART assessment.

II.2.4.3) Hospital Anxiety and Depression Scale

Mood was assessed using the HADS (Zigmond and Snaith, 1983). The HADS was developed to minimise the difficulties associated with using a scale to measure anxiety and depression in a chronic disease population. Measures of anxiety and depression contain assessments of fatigue, insomnia and change in appetite as indicators of mood. In the chronic pain population these symptoms may frequently occur as a result of the physical symptoms due to underlying disease. The HADS overcomes some of these problems and may be the best indicator of mood available (Zigmond and Snaith, 1983). This assessment cannot accurately determine psychiatric clinical mood disorder but instead is used to indicate negative affectivity in these domains. This use is consistent with the majority of research on mood states in pain.

The HADS consists of seven anxiety and seven depression related items that are administered as alternating items. The two subscales when scored will be referred to as Total Anxiety (HADS) and Total Depression (HADS).

II.2.4.4) Chicago Multiscale Depression Inventory

The Chicago Multiscale Depression Inventory (CMDI) (Nyenhuis et al., 1998) was also used to assess mood. This measure consists of 50 word or phrases. Each participant determines the degree to which each word or phrase describes them during the past week, including today. In scoring, the items are split into three groups: mood, evaluative, vegetative. This measure has been validated on an MS population (Chang et al., 2003).

II.2.4.5) European Database for Multiple Sclerosis Scale

A score was assigned for each participant for level of disability using the European Database for Multiple Sclerosis (EDMUS) evaluation (Grimaud et al., 1999) which is similar to the Expanded Disability Severity Score (EDSS) (Kurtzke, 1983). The EDSS has been validated against patients' own assessment of disability (Verdier-Taillefer et al., 1994). The EDMUS is a ten-point scale with 0 being a completely normal neurological score t 10 being death due to MS. Since the higher end of the scale is characterised by level of ambulation, patients were able to self-identify their own placement on the scale.

II.2.5) ASSESS THE DEGREE OF EMOTIONAL DISTRESS IN THIS STUDY POPULATION AND ITS RELATIONSHIP TO PAIN

II.2.5.1) Coping with Multiple Sclerosis Scale

Patients were asked to complete the Coping with Multiple Sclerosis Scale (CMSS) (Pakenham, 2001) in order to determine how this population dealt with pain. The CMSS consists of eight subscales. **Acceptance** subscale involves accepting MS and using humour to deal with difficult situations. **Social Support** is seeking out support of others. **Energy Conservation** involves using rest and other energy conservation strategies. **Emotional Release** involves trying to understand feelings and letting out those feelings. **Problem Solving** involves focusing on the present and addressing the problem from a practical rather than emotional standpoint. **Physical Assistance** refers to taking advantage of necessary physical and other assistance. **Avoidance** involves attempting to

avoid the problems and keep others unaware of them. **Personal Health Control** involves attempting to promote one's own wellness.

In terms of scoring, the CMSS is made up of 43 question scored from 0-4. Points per subscale are as follows:

Acceptance consists of 6 items (maximum possible score = 24).

Social support consists of 2 items (maximum possible score = 8).

Energy conservation consists of 4 items (maximum possible score = 16).

Emotional release consists of 6 items (maximum possible score = 24).

Problem solving consists of 5 items (maximum possible score = 20).

Physical assistance consists of 5 items (maximum possible score = 20).

Avoidance consists of 4 items (maximum possible score = 16).

Personal health control consists of 4 items (maximum possible score = 16).

Not all items are included in the subscales.

II.2.5.2) Multiple Sclerosis Impact Scale

The Multiple Sclerosis Impact Scale (MSIS) (Riazi et al., 2002) was given to participants to assess HQOL. This measure consists of a total of twenty-nine questions with the first twenty measuring **physical issues** and the remaining nine measuring **emotional issues**. For each question, the patient is asked to respond with not at all, a little, moderately, quite a bit or extremely (1-5 respectively). The maximum possible impact score therefore is 145 with maximum possible physical impact score being 100 and the maximum possible emotional impact score being 45.

II.2.5.3) Fatigue Impact Scale

Fatigue of participants was measured using the Fatigue Impact Scale (FIS) (Fisk et al., 1994). The FIS has specifically been designed and validated in the MS population (Fisk et al., 1994). The FIS consists of forty questions that are subdivided into three areas of impact: Cognitive (10 questions), Physical (10 questions) and Social (20 questions). For each statement the patient is asked to endorse: no problem, small problem, moderate problem, big problem or extreme problem (0-4 respectively). This scale has a maximum possible score of 160 with maximum cognitive impact score of 40, maximum physical impact score of 40 and maximum social impact score of 80.

II.3) Study Population – DEMOGRAPHICS

This study was performed using an outpatient population and therefore this population should be representative of the SP and PP MS populations in a large tertiary urban hospital. There are two major studies had that may be expected to have similar samples: Vermote et al., 1986 and Archibald et al., 1994. The Vermote et al. study used a hospitalised population. Vermote at al. 1986 stated that their population might not be representative of MS patients overall as these patients were hospitalised for rehabilitation and their pain may have been part of the basis for this hospitalisation (Vermote et al., 1986). The Vermote study may be biased towards patients with pain where the pain was viewed as amenable to rehabilitation. The Archibald sample was a sample from a regional referral clinic (Archibald et al., 1994) so this sample may be a more similar comparison group to the current study.

However, it should be acknowledged that the Queen Square National Hospital is a tertiary care referral facility. This means that patients encountered are likely to have more severe disease than patients in a district general hospital or those in a community sample. When considering comparisons with different research studies it is important to keep in mind that referral patterns may be different in different countries due to availability of long-term care and awareness of general practitioners (GPs) and other health professionals of pain problems. There are also differences with regard to patient education and assertiveness in different cultures. Additionally, there are differences with regard to treatment availability and payment for such treatment by different healthcare structures.

II.3.1) INDIVIDUAL MEASURES FOR ALL PARTICIPANTS

The study participants were similar on disability status, gender and age to people with MS who are classified as SP or PP although they may be slightly older given the hospital nature of their affiliation.

In Sections II.3.1.1 through II.3.1.4, measures will be described with the results for the study participants and, where possible, with other published MS samples.

II.3.1.1) Gender

Gender distribution was as expected for a sample consisting of limited to SP and PP. SP has a gender distribution with a higher proportion of women than men. For PP the gender ratio is 1:1. So with 60 women to 42 men, this ratio fits expectations, as shown in Table II.3.1.1.

TABLE II.3.1.1) GENDER DISTRIBUTION

N=102	Frequency (%)
F	60 (58.8)
M	42 (41.2)

II.3.1.2) Type of MS

Subtypes were about what was expected, given the overall incidence of SP (24%) vs. PP (18%) as shown in Table II.3.1.2. However, there may have been a few excess PP participants, as recruitment for PP was facilitated by recruitment through another unrelated imaging study.

TABLE II.3.1.2) MS SUBTYPE DISTRIBUTION

N=102	Frequency (%)
SP	60 (58.8)
PP	42 (41.2)

II.3.1.2.1) TYPE OF MS by Gender

Type of MS by gender is similar to ratios found by others. McDonald and Ron report a female to male ratio of 3:1 for SP and 1:1 for PP whereas PP would be 1:1. Since we had 60 SP and 42 PP, we would expect that 21 of the PP would be women and 45 of the SP would be women. The total of women

therefore should be 66. Instead, we found 60 rather than 66 but this is not large variation from the predicted ratio, as shown in Table II.3.1.2.1

TABLE II.3.1.2.1) MS SUBTYPE BY GENDER DISTRIBUTION

	F	M
PP	19	23
SP	41	19

II.3.1.3) Age

Age (mean=51, range=29-73) was as expected given that participants were SP or PP. Age was not an exclusion criterion. Since the participants were all affiliated with a tertiary facility, a slightly older age distribution may be expected, as shown in Table II.3.1.3.

TABLE II.3.1.3) AGE DISTRIBUTION

N=102	Minimum	Maximum	Mean	SD
Age	29.32	73.26	51.36	9.11

II.3.1.4) Disability

Level of disability was not an inclusion or exclusion criterion and, given age and disease subtype, the level of disability fits expectation (McDonald and Ron, 1999), as shown in Table II.3.1.4.A-B. The study population is more significantly disabled than most samples used in previous studies on pain in MS, e.g., Vermote et al (1986) described their population as 'rather severely disabled' as 80% required assistance for walking or were even more disabled. In this study, 85.3% required at least one stick for walking or even more assistance. Since recruited participants were SP or PP MS, with a mean age of 51 years, this level of disability is not surprising.

TABLE II.3.1.4.A) EDMUS DISTRIBUTION

N=102	Minimum	Maximum	Mean	SD
EDMUS	2.00	8.00	6.35	1.41

TABLE II.3.1.4.B) FREQUENCY TABLE OF EDMUS

N=102 EDMUS score	Frequency	Cumulative percent
2.0	3	2.9
3.0	4	6.9
4.0	3	9.8
5.0	5	14.7
6.0	29	43.1
6.5	20	62.7
7.0	15	77.5
8.0	23	100.0

II.3.2) COGNITIVE BIAS MEASURES –Experimental tasks

As the following tasks have not been previously used with an MS sample, typicality cannot be determined.

II.3.2.1) Stem Completion Task

Certain stems produced many fewer words, as shown in Table II.3.2.1.B and C. This may be due to overwhelming bias towards the obvious choices, (i.e., HOS producing hospital, as this was the location in which they were asked to produce the words). However, since the minimum number of different words produced for a stem was 20, as shown in Table II.3.2.1.A, there were clearly adequate accessible possibilities from which to choose.

TABLE II.3.2.1.A) STEM COMPLETION WORDS

N=102	Minimum	Maximum	Each stem
Words	20	98	39.875

TABLE II.3.2.1.B) STEM COMPLETION SEMANTIC DISTRIBUTION

N=102 Semantic Category	Possible maximum	Minimum	Maximum	Mean	SD
Neutral	32	17	31	23.90	2.65
Sensory pain		0	6	1.86	1.31
Affective pain		0	5	2.03	1.05
Illness		0	8	3.51	1.54
MS		0	3	0.70	0.77

TABLE II.3.2.1.C) STEM COMPLETION TASK MEANS TESTING (T-TEST)

N=102	Mean	SD	t	Sig. (2-tailed)
Sensory Affective	1.86 2.03	1.31 1.05	-1.06	.291
Sensory Illness	1.86 3.51	1.31 1.54	**-8.61****	**<.001**
Sensory MS	1.86 0.70	1.31 0.77	**7.71****	**<.001**
Affective Illness	2.03 3.51	1.05 1.54	**-8.18****	**<.001**
Affective MS	2.03 0.70	1.05 0.77	**11.25****	**<.001**
Illness MS	3.51 0.70	1.54 0.77	**17.33****	**<.001**

(*p<0.05, **p<0.01)

II.3.2.2) Experimental Recall Learning Task

Sensory pain words had significantly higher recall than neutral, affective, and MS words as shown in Table II.3.2.2.A. In simply determining overall recall capability, recall was as expected, given scores on the CVLT which uses a very similar structure.

TABLE II.3.2.2.A) EXPERIMENTAL RECALL TASK RESPONSES

n=102	Possible Maximum	Minimum	Maximum	Mean	SD
Correct responses	100	3	60	28.23	10.79
Perseverations		0	16	2.99	3.02
Intrusions		0	13	3.61	2.83

TABLE II.3.2.2.B) EXPERIMENTAL RECALL TASK RESPONSE ORDER

n=102	Minimum	Maximum	Mean	SD
Primary words	0	17	8.82	4.16
Secondary	0	29	8.84	5.67
Recency	2	20	10.56	4.32
Serial	0	22	3.46	2.98

TABLE II.3.2.2.C) EXPERIMENTAL RECALL TASK SEMANTIC DISTRIBUTION

n=102	Minimum	Maximum	Mean	SD
Leading/Following	3	19	10.79	3.94
Neutral	0	10	3.82	2.53
Sensory pain	0	13	5.23	2.83
Affective pain	0	14	4.15	3.31
MS	0	15	4.24	2.87

TABLE II.3.2.2.D) EXPERIMENTAL RECALL TASK SEMANTIC MEANS TESTING (T-TEST)

N=102	Mean	SD	t	Sig.
Neutral	3.82	**3.82**	**-4.21****	**<.001**
Sensory	5.23	**5.23**		
Neutral	3.82	3.82	-1.08	.281
Affective	4.15	4.15		
Neutral	3.82	3.82	-1.24	.216
MS	4.24	4.24		
Sensory	5.23	**5.23**	**3.20****	**.002**
Affective	4.15	**4.15**		
Sensory	5.23	**5.23**	**3.11****	**.002**
MS	4.24	**4.24**		
Affective	4.15	4.15	-0.26	.795
MS	4.24	4.24		

(*p<0.05, **p<0.01)

II.3.2.3) Hayling Sentence Completion Task

Participants completing congruous pain sentences were significantly slower than congruous non-pain sentences whereas time to complete incongruous pain sentences was not significantly different from incongruous non-pain, as shown in Table II.3.2.3.A. & B. Incongruous stems may produce more variation so that this lack of difference may not relate to whether the stem is a pain or non-pain lead.

There were significantly more errors made in the pain related sentences than in the non-pain related sentences, as shown in Table II.3.2.3.C & D.

TABLE II.3.2.3.A) HAYLING SENTENCE COMPLETION RATES

time in 1/100s	Minimum	Maximum	Mean	SD
Congruous Pain	.37	7.47	1.23	0.86
Congruous non-pain	.39	6.11	0.95	0.64
Incongruous Pain	.39	13.16	3.20	2.27
Incongruous non-pain	.43	11.67	3.42	2.17

TABLE II.3.2.3.B) COMPARISONS OF MEANS

N=102	Mean	t	Sig.
Congruous pain Congruous non-pain	**1.23** **0.95**	**5.56****	**<.001**
Incongruous pain Incongruous non-pain	3.20 3.42	-1.85	.068
Congruous pain Incongruous pain	**1.23** **3.20**	**-10.86****	**<.001**
Congruous/Incongruous non-pain	**0.95** **3.42**	**-12.83****	**<.001**

(*p<0.05, **p<0.01)

TABLE II.3.2.3.C) HAYLING SENTENCE COMPLETION TASK ERROR MEANS

Sentence type	Minimum errors	Maximum Errors	Mean errors	SD of errors
Pain	0	14	3.96	3.08
Non-pain	0	16	3.94	3.39
Type A pain	0	7	0.84	1.49
Type Anon-pain	0	8	0.80	1.30
Type B pain	0	6	2.27	1.56
Type B non-pain	0	7	2.33	1.84
A pain rate	.00	1.00	0.120	0.21
A non-pain rate	.00	1.00	0.101	0.16
B pain rate	.00	0.86	0.325	0.22
B non-pain rate	.00	0.88	0.292	0.23

TABLE II.3.2.3.D) HAYLING SENTENCE COMPLETION MEANS TEST (T-TEST)

N=102	Mean	t	Sig. (2-tailed)
Pain error Non-pain error	**.57** **.49**	**2.63***	**.010**
Type B pain error rate Type A pain error rate	**.33** **.12**	**6.13****	**<.001**
Type B non-pain error rate Type A non-pain error rate	**.29** **.10**	**7.41****	**<.001**
Type A pain error rate Type A error non-pain rate	.12 .10	1.47	.145
Type B pain error rate Type B non-pain error rate	.33 .29	1.57	.119

(*p<0.05, **p<0.01)

II.3.3) PAIN SELF-REPORT MEASURES

In terms of incidence and qualitative aspects of pain, the current sample is similar to previously published samples. Details by measure follow in Sections II.3.3.1 & 2.

II.3.3.1) SD

The disease portion of the SD showed that participants on the whole rated themselves as fairly disabled and fairly fatigued, as shown in Table II.3.3.1.A

through II.3.3.1.G. Given the EDMUS scores that most walked with at least one aid, we would expect that this population would rate themselves as disabled. Overall, fatigue is a common symptom in the MS population and we would expect that fatigue would be a significant symptom. For disability and fatigue, the current sample participants rated themselves in line with objective evaluations.

For the "comfortable" vs. "in pain" question, 17% stated that they had no pain and 82% stated that they were not completely pain free. Fifty-six were at the midpoint between "comfortable" vs. "in pain," or closer to "in pain". This percentage is similar to what Archibald et al. (1994) found for patients reporting pain. They found 53% reported pain using a structured pain interview. However, it is possible that our study found a slightly higher prevalence due to a different MS subtype breakdown and more significant disability of EDMUS=6.35 (Archibald et al.'s mean EDSS was 4.2).

Vermote et al (1986) found that 54.2% experienced pain (as determined by record report) however, they excluded pain types: headache or visceral pain. Again, this prevalence is close to what was found here despite this difference in measurement.

TABLE II.3.3.1.A) EMOTIONAL AND DISEASE SD OVERALL MEAN

N=102	Minimum	Maximum	Mean	SD
Total Emotional	0	44	19.59	8.81
Total Disease	2	19	10.87	3.55

TABLE II.3.3.1.B) DISEASE SD QUESTIONS

N=102	Minimum	Maximum	Mean	SD
Healthy vs. Ill	0	4	2.02	1.22
Able-bodied vs. Disabled	0	4	2.77	1.09
Comfortable vs. In pain	0	4	1.71	1.17
Energetic vs. Fatigued	0	4	2.54	1.09
Pain: treatable vs. Non-treatable	0	4	1.83	1.30

TABLE II.3.3.1.C) HEALTHY VS. ILL FREQUENCY TABLE

N=102	0	1	2	3	4
Frequency (%)	10 (9.8)	29 (28.4)	27 (26.5)	21 (20.6)	15 (14.7)

TABLE II.3.3.1.D) ABLE-BODIED VS. DISABLED FREQUENCY TABLE

N=102	0	1	2	3	4
Frequency (%)	2 (2.0)	15 (14.7)	17 (16.7)	38 (37.3)	30 (29.4)

TABLE II.3.3.1.E) COMFORTABLE VS. IN PAIN FREQUENCY TABLE

N=102	0	1	2	3	4
Frequency (%)	18 (17.6)	27 (26.5)	31 (30.4)	19 (18.6)	7 (6.9)

TABLE II.3.3.1.F) ENERGETIC VS. FATIGUED FREQUENCY TABLE

N=102	0	1	2	3	4
Frequency (%)	4 (3.9)	13 (12.7)	31 (30.4)	32 (31.4)	22 (21.6)

TABLE II.3.3.1.G) PAIN: TREATABLE VS. NON-TREATABLE FREQUENCY TABLE

N=102	0	1	2	3	4
Frequency (%)	23 (22.5)	14 (13.7)	34 (33.3)	19 (18.6)	12 (11.8)

II.3.3.2) McGill Scale

The adjectives chosen in this study were similar to those chosen in other studies using an MS population. The adjectives chosen are given in Tables II.3.3.2.A though D. Vermote et al. found that persistent extremity pain was the

most common neurogenic pain type (Vermote et al., 1986). This type of pain is usually described by McGill adjectives including pricking, tingling, dull. Painful tonic spasms were the second most common neurogenic pain type found by Vermote et al (1986). This type of pain is typically described by McGill adjectives cramping, tugging and pulling. In our study we found more reports falling into the category of the painful tonic spasms followed by those falling into persistent extremity pain. However, Vermote et al did find that painful tonic spasms increased with increasing disability and this may be why this pain type was particularly common overall in our group, as ours was limited to SP and PP MS.

TABLE II.3.3.2.A) FREQUENCY TABLE FOR NUMBER OF CATEGORIES SELECTED ON MCGILL

Response	Percent	Cumulative percent
0	2.9	2.9
1	2.9	5.9
2	3.9	9.8
3	1.0	10.8
4	5.9	16.7
5	5.9	22.5
6	6.9	29.4
7	2.9	32.4
8	8.8	41.2
9	5.9	47.1
10	5.9	52.9
11	10.8	63.7
12	7.8	71.6
13	4.9	76.5
14	6.9	83.3
15	4.9	88.2
16	3.9	92.2
17	2.0	94.1
18	1.0	95.1
19	1.0	96.1
20	3.9	100.0

TABLE II.3.3.2.B) MCGILL ITEM FREQUENCY TABLE IN DESCENDING POPULARITY OF INDIVIDUAL ADJECTIVES

N=102	Frequency		Frequency		Frequency
Exhausting	44	Tight	13	Crushing	7
Cramping	37	Boring	12	Searing	6
Heavy	37	Stabbing	12	Sore	6
Tiring	37	Stinging	12	Cutting	6
Numb	36	Gruelling	12	Pulling	6
Nagging	32	Miserable	12	Hurting	6
Throbbing	31	Radiating	12	Squeezing	6
Annoying	28	Cool	12	Nauseating	6
Tingling	27	Gnawing	11	Pinching	5
Aching	24	Unbearable	11	Frightful	5
Cold	24	Torturing	11	Flashing	4
Shooting	23	Wrenching	10	Smarting	4
Sharp	22	Quivering	10	Vicious	4
Taut	21	Dull	10	Dreadful	4
Burning	19	Piercing	10	Cruel	4
Tender	19	Penetrating	10	Blinding	4
Hot	19	Splitting	9	Tearing	4
Jumping	18	Spreading	9	Killing	3
Itchy	17	Agonising	9	Lacerating	2
Pricking	17	Pulsing	8	Scalding	2
Fearful	15	Tugging	8	Drawing	2
Troublesome	15	Terrifying	8	Beating	1
Intense	15	Suffocating	8	Drilling	1
Sickening	14	Flickering	7	Lancinating	1
Punishing	14	Pressing	7	Rasping	0

TABLE II.3.3.2.C) MCGILL CATEGORY FREQUENCY TABLE

N=102	Frequency (%)		Frequency (%)
Category 1	61 (59.8)	Category 11	81 (79.4)
Category 2	45 (44.1)	Category 12	22 (21.6)
Category 3	43 (42.2)	Category 13	28 (27.5)
Category 4	30 (29.4)	Category 14	37 (36.3)
Category 5	67 (65.7)	Category 15	20 (19.6)
Category 6	24 (23.5)	Category 16	81 (79.4)
Category 7	46 (45.1)	Category 17	41 (40.2)
Category 8	60 (58.8)	Category 18	61 (59.8)
Category 9	83 (81.4)	Category 19	46 (45.1)
Category 10	49 (48.0)	Category 20	62 (60.8)

II.3.3.3) Pain Discomfort Scale

The scores for the Pain PD scale and the Discomfort PD scale were not significantly different (t= -0.546, p= 0.586) as shown in Table II.3.3.3. This is unsurprising given the similarity of the structure and wording of the assessment. However, there were enough exceptions by participant to warrant examination of these measures independently.

TABLE II.3.3.3) PAIN AND DISCOMFORT SCALE SCORE

N=102	Minimum	Maximum	Mean	SD
Total Pain	0	36	12.23	8.22
Total Discomfort	0	36	12.48	8.50

II.3.3.4) SOPA

The SOPA was based on the 84 people who stated they did have some pain on the SD. See section II.2.3.4 for a description of this measure.

The SOPA consists of seven subscales: control, disability, harm, emotion, medication, solicitude, and medical cure. All of these mean scores are shown in Table III.3.3.4.

The means were about at the median of the possible range of scores, with the exception of disability. Given that this study population was significantly

disabled, this is as expected as given within ranges of disabled populations (non-MS).

TABLE II.3.3.4) SOPA SUBGROUP MEANS

N=84	Maximum possible score	Minimum	Maximum	Mean	SD
Control	40	0	31	18.29	6.24
Disability	40	0	39	20.24	7.26
Harm	32	0	27	15.42	5.61
Emotion	32	0	24	13.94	5.97
Medication	24	0	24	15.61	5.27
Solicitude	24	0	24	8.75	5.90
Medical Cure	36	0	31	16.70	5.76

II.3.4) GENERAL COGNITIVE ASSESSMENT

On tests of cognitive function, the current sample was generally similar to previous studies.

II.3.4.1) CVLT

The published mean and standard deviation for an MS population on the total free recall score summed across five trials is mean=40.6, SD=15.8 (Delis et al., 1987). The current study data are shown in Table II.3.4.1. The mean found in this study is close (not significantly different) to that found for the previous sample (t=-0.478, p=0.63). This suggests that the current sample is typical of other MS research samples with regard to cognitive impairment.

TABLE II.3.4.1) CVLT SCORES

N=102	Possible maximum	Minimum	Maximum	Mean	SD
Total correct	80	11	66	39.55	11.53
Total perseverations		0	20	4.02	3.97
Total intrusions		0	11	1.52	2.23
Total semantic cluster	60	0	44	9.15	7.98
Total serial cluster	75	0	19	4.55	3.37
Primary percent		0.09	0.60	0.29	0.08
Secondary percent		0.00	0.60	0.36	0.11
Recency percent		0.05	0.75	0.35	0.11

II.3.4.2) NART

A study by Camp (Camp, 2000) using the NART with 100 patients found a mean error score of 20.24 (SD=10.98) and an IQ score of 105.62 (SD - 13.60). Median (range) is 107.50 (70-129) and 95% confidence limits 102.91-108.33. The current study found a mean error score of 16.0 out of 50 words, as shown in Table II.3.4.2, which equates to an IQ score of 111. Since the score for the current study is within one standard deviation of the mean IQ for the Camp study, it appears that the current population is not significantly different from the Camp population. This is not surprising, as the NART is designed to assess premorbid IQ, and it would be expected that premorbid IQ would be fairly consistent for the Queen Square study population.

TABLE II.3.4.2) NART NUMBER OF ERRORS (X/50)

N=98	Maximum possible number of errors	Minimum	Maximum	Mean	SD
NART	50	0	45	16.03	10.10

II.3.5) EMOTIONAL ASSESSMENT

Overall, the scores of the current sample on measures of mood are broadly comparable to other published studies. Specific measures will be discussed in Sections II.3.5.1 through II.3.5.2

II.3.5.1) HADS

II.3.5.1.1) Anxiety

Clinically significant anxiety (HADS anxiety>10) was evident in 25% of the population. Borderline anxiety accounted for 18% (HADS anxiety 8-10). The percentage of the study population with clinically significant anxiety is the same as found in the Feinstein study (25%) (Feinstein et al., 1999) despite the use of different anxiety measures.

TABLE II.3.5.1.1) HADS ANXIETY

N=102	<8	8 ≤ x ≤10	>10
Frequency (%)	59 (57.8)	18 (17.6)	25 (24.5)

II.3.5.1.2) Depression

Clinically significant depression (HADS depression >10) was evident in 16% of the population. Borderline depression accounted for 18%. Another study found 17% could be diagnosed with major depression (Feinstein and Feinstein, 2001). The clinically significant depression populations are very close, despite different depression measures being used.

TABLE II.3.5.1.2) HADS DEPRESSION

N=102	<8	8 ≤ x ≤10	>10
Frequency (%)	68 (66.7)	18 (17.6)	16 (15.7)

II.3.5.1.3) Comorbidity of HADS anxiety and depression

Of those who had an anxiety score of 8 or more, 37.2% did not have associated depression, 20.9% had borderline depression and 41.8% had significant depression, as shown in Table II.3.5.1.3.A.

Of those who had a depression score of 8 or more, 20.6% did not have associated anxiety. 38.2% had borderline anxiety as well and 41.2% had significant anxiety, as shown in Table II.3.5.1.3.B. Therefore, as in the study by Feinstein (Feinstein et al., 1999), depression more commonly occurred alongside anxiety whereas anxiety was more likely to occur alone.

TABLE II.3.5.1.3.A) HADS BORDERLINE OR GREATER ANXIETY (8 OR GREATER) BY DEPRESSION (N (%))

		Depression		
Anxiety (≥8)	N=43	<8	8 ≤ x ≤10	>10
	Frequency (%)	16 (37.2)	9 (20.9)	18 (41.8)

TABLE II.3.5.1.3.B) HADS BORDERLINE OR GREATER DEPRESSION (8 OR GREATER) BY ANXIETY (N (%))

		Anxiety		
Depression (≥8)	N=34	<8	8 ≤ x ≤10	>10
	Frequency (%)	7 (20.6)	13 (38.2)	14 (41.2)

II.3.5.2) Self Reported Scale of Emotion – CMDI

The mean scores for mood (14 questions), evaluative (14 questions) and vegetative (14 questions) were 28.04, 23.99 and 38.02 respectively. The mean scores for the three subgroups (mood, evaluative, vegetative) were significantly different for each comparison with vegetative having the highest mean, mood being in the middle and evaluative having the lowest mean, as shown in Table II.3.5.2.A.

If we analyse the means for each of these categories after the method of Nyenhuis et al.: mood (9 questions), evaluative (6 questions) and vegetative (9 questions), the current sample performed similarly (not significantly different) on the CMDI to the Chang et al. (Chang et al., 2003) MS sample for mood (t=1.10, p=0.27) and evaluative (t=1.80, p=0.072) subscales, as shown in Table II.3.5.2.B. However, the current sample performed differently on the vegetative scale, with the Chang sample having a significantly different mean (t=2.48, p=0.013), indicating less depressive mood of the vegetative type. This difference may be

due to the fact that the Chang sample was approximately half RR. Additionally, although EDSS was not reported for the Chang sample it is likely that this sample was not as disabled as the current sample. The vegetative subscale includes fatigue; sleep disturbance and cognitive issues, which may be more severe in patients whose disability is more severe.

However, in general, the current sample means are similar to those obtained in other studies using the CMDI in large MS samples.

TABLE II.3.5.2.A) CMDI MEANS

	Possible maximum	Minimum	Maximum	Mean	SD
Total	210	44	177	90.05	30.14
Mood	70	14	63	28.04	12.91
Evaluative	70	14	66	23.99	11.45
Vegetative	70	14	67	38.02	10.19

TABLE II.3.5.2.B) CMDI MEANS (ANALYSED AS IN NYENHUIS ET AL. 1998)

	Possible maximum	Minimum	Maximum	Mean	SD
Total (24 item)	120	25	98	53.95	17.17
Mood (9 item)	45	9	40	18.56	8.49
Evaluative (6 item)	30	6	28	9.86	4.82
Vegetative (9 item)	45	9	44	25.53	7.17

II.3.6) ASSESSMENT OF OTHER CONTRIBUTING FACTORS

The current sample reported impact of MS and fatigue on their lives, and their general coping levels to be similar to those of other published, comparable samples. Data from individual measures will be given in Sections II.3.6.1 to 3.

II.3.6.1) MS Impact Scale

The mean for the entire sample on the physical subscale (62.11) of the MS impact scale falls within the range for different patient subsamples (rehabilitation, hospitalised for treatment, etc) (67 to 56) used in the Riazi et al. (Riazi et al., 2002) study. This is appropriate as these were specialized samples but in the current study a more general outpatient sample was used. The emotional subscale mean (38.21) also falls within the range for the means of the different samples in the Riazi et al 2002 study (47.3 to 34.3).

TABLE II.3.6.1) MSIS SUBSCALE SCORES

N=102	Maximum possible	Minimum	Maximum	Mean	SD
Physical	100	21	99	62.11	18.76
Emotional	45	9	42	38.21	22.84

II.3.6.2) Fatigue Impact Scale

The means of the cognitive, physical and social subscales and total were not statistically different than those found in the Fisk et al. (Fisk et al., 1994) study respectively ((t=-1.376, p=0.17), (t-0.55, p=0.59), (t=-1.06, p=0.29) and (t=–0.804, p= 0.42) respectively) (Fisk et al., 1994). Therefore, the means from this sample do not appear to be different from other MS samples and therefore the current sample is reporting a similar level of fatigue to participants of other published studies.

TABLE II.3.6.2) FIS SUBSCALE MEANS

	Maximum possible	Minimum	Maximum	Mean	SD
Total cognitive function	40	0	37	12.53	9.89
Total physical function	40	0	37	20.57	9.05
Total social function	80	0	73	29.55	17.74
Total	160	0	146	62.55	33.94

II.3.6.3) Coping with MS Scale

The most highly endorsed subscale was acceptance followed by problem solving, energy conservation, avoidance, and emotional release. This was also true of the Pakenham sample (Pakenham, 2001), although the subscale, physical assistance, jumped ahead of personal health control in our sample. This may have been due to the fact that our sample included no RR subtype and Pakenham had 62% RR. Therefore our sample was more disabled and would be expected to require more physical assistance, solely based on mobility needs.

TABLE II.3.6.3.A) CMSS SUBGROUP SCORES

	Maximum possible	Minimum	Maximum	Mean	SD
Acceptance	24	7	24	16.26	3.57
Social support	8	0	8	3.25	1.99
Energy conservation	16	2	16	10.05	3.12
Emotional release	24	0	22	12.01	4.11
Problem solving	20	2	20	13.46	3.65
Physical assistance	20	0	18	8.69	4.04
Avoidance	16	3	16	9.33	2.69
Personal health control	16	0	13	5.43	3.12
Total subscale score	144	41	114	78.48	15.08
Total score	172	47	134	90.34	17.66

TABLE II.3.6.3.B) CMSS SUBGROUP MEANS CALCULATED ACCORDING TO PAKENHAM (2001)

	Maximum possible	Minimum	Maximum	Mean	SD
Acceptance	4.00	1.17	4.00	2.71	0.59
Social support	4.00	0.00	4.00	1.62	0.99
Energy conservation	4.00	0.50	4.00	2.51	0.78
Emotional release	4.00	0.00	3.67	2.00	0.69
Problem solving	4.00	0.40	4.00	2.69	0.73
Physical assistance	4.00	0.00	3.60	1.74	0.81
Avoidance	4.00	0.75	4.00	2.33	0.67
Personal health control	4.00	0.00	3.25	1.36	0.78

II.4) RELATIONSHIPS BETWEEN VARIABLES - Subscales and related measures

II.4.1) DEMOGRAPHICS AND DISEASE VARIABLES

II.4.1.1) Gender Correlations

Gender correlations with EDMUS score, total McGill score, total McGill adjectives, HADS depression, HADS anxiety, emotional SD, illness SD and comfortable/in pain SD were examined yet none were significantly correlated. This was not surprising since the sample itself was relatively homogenous in terms of disease status and this may have disguised any relationship that may appear in wider MS samples. Previous studies have often not found a significant difference by gender in terms of reporting pain or not reporting pain (Stenager et al., 1991; Archibald et al., 1994).

For future reference, it may be important to consider the gender distribution by MS subtype, as shown in table II.4.1.1.

TABLE II.4.1.1) MS SUBTYPE BY GENDER DISTRIBUTION

N=102	F	M
SP (0)	41	19
PP (1)	19	23

II.4.1.2) Age Correlations

The only significant negative correlation was between emotional SD and age, as shown in Table II.4.1.2. Pain has been found to be unrelated to age (Stenager et al., 1991; Archibald et al., 1994). They did find a difference between disease duration and neurological severity and number of pain hours per week but not with pain severity or number of pain sites (Archibald et al., 1994).

With advancing age, people showed less negative emotion. This may be evidence of the ability to adapt and accept the MS diagnosis with time. This result may be similar to the finding that people who have been diagnosed longer, have a better quality of life (Ford et al., 2001).

TABLE II.4.1.2) CORRELATIONS BETWEEN AGE AND OTHER FACTORS

N=102		Age
EDMUS	Pearson corr.	.044
	Sig. (2-tailed)	.660
McGill Adj.	Pearson corr.	-.060
	Sig. (2-tailed)	.547
Total McGill score	Pearson corr.	-.134
	Sig. (2-tailed)	.180
Emotional SD	Pearson corr.	**-.200***
	Sig. (2-tailed)	**.044**
Disease SD	Pearson corr.	-.050
	Sig. (2-tailed)	.618
Comfortable vs. In Pain	Pearson corr.	-.035
	Sig. (2-tailed)	.724

(*p<0.05, **p<0.01)

II.4.1.3) Type of MS Correlations

Significant negative correlations were demonstrated between MS subtype and HADS Anxiety, HADS Total and Emotional SD as shown in Table II.4.1.3. People who were PP MS showed less negative emotion. This may be similar to the finding of a relationship between psychological well being and subtype of MS (Vleugels et al., 1998) and may speak to **hypothesis 2** where SP patients do have more anxiety. However, total McGill score was not correlated with MS

subtype. Archibald et al. 1994 did not find a difference between types of MS and reporting or not reporting pain (Archibald et al., 1994). If the data are examined in the same way, using the SD for comfortable vs. in pain, no significant difference appears here either.

TABLE II.4.1.3) MS SUBTYPE BY OTHER FACTORS

N=102		MS subtype
EDMUS	Pearson corr.	-.168
	Sig. (2-tailed)	.091
McGill Adj.	Pearson corr.	-.191
	Sig. (2-tailed)	.055
Total McGill score	Pearson corr.	-.131
	Sig. (2-tailed)	.191
HADS Anxiety	Pearson corr.	**-.206***
	Sig. (2-tailed)	**.037**
HADS Depression	Pearson corr.	-.162
	Sig. (2-tailed)	.103
HADS Total	Pearson corr.	**-.207***
	Sig. (2-tailed)	**.037**
Emotional SD	Pearson corr.	**-.211***
	Sig. (2-tailed)	**.034**
Disease SD	Pearson corr.	-.167
	Sig. (2-tailed)	.093
Comfortable vs. In Pain	Pearson corr.	-.028
	Sig. (2-tailed)	.778

(*p<0.05, **p<0.01)

II.4.1.4) Disability Correlations

The only significant correlation between disability and other factors was for Disease SD, as shown in Table II.4.1.4. People who were more disabled showed more negative disease related effects but not more negative emotional factors. This may mean that more disabled people experience more disease related factors rather than more emotional factors or perhaps just that disease related factors are more profoundly increased as compared to emotional factors. In other studies, increasing disability is also not necessarily correlated with a

decrease in quality of life (Ford et al., 2001). This is similar to several previous studies, as EDSS or similar measures, with disability status not being significantly different for pain vs. non-pain reporters (Stenager et al., 1991; Archibald et al., 1994; Rae-Grant et al., 1999). In addition, there has been evidence that scales like the EDMUS are not designed to be able to detect disability with adequate precision (Nortvedt et al., 1999) so this lack of a significant difference may be expected.

TABLE II.4.1.4) EDMUS BY OTHER FACTORS

N=102		EDMUS
McGill Adj.	Pearson corr.	.089
	Sig. (2-tailed)	.376
Total McGill score	Pearson corr.	.080
	Sig. (2-tailed)	.422
Emotional SD	Pearson corr.	-.022
	Sig. (2-tailed)	.983
Disease SD	Pearson corr.	**.234***
	Sig. (2-tailed)	**.018**
Comfortable vs. In Pain	Pearson corr.	.142
	Sig. (2-tailed)	.154

(*p<0.05, **p<0.01)

II.4.2) COGNITIVE BIAS VARIABLES

There were no significant correlations between CVLT groups (high/low) or by NART groups (high/low) and the stem completion task. The ERLT and the Hayling did show some relationships and these are displayed in tables II.4.2.1-4.

II.4.2.1) CVLT and ERLT

The two measures CVLT and ERLT are fairly similar measures with similar structure. The cognitive efficiency of memory processes should be broadly comparable for both neutral and more salient stimuli words. However, the means for correct responses, perseverations and intrusions were statistically different, as shown in Table II.4.2.1. The CVLT had a higher mean for correct responses and perseverations whereas; the ERLT had a higher intrusion score. As the ERLT contains a longer list (N=20) than the CVLT (N=16) and the ERLT uses more

reactive words, it is possible that these factors account for these differences. Words on the CVLT may be more familiar to the general public (leading to more correct recall) and the ERLT may provoke the listener to produce similar semantic words (more intrusions).

TABLE II.4.2.1) COMPARISON BETWEEN CVLT AND EXPERIMENTAL RECALL TASK (T-TEST)

N=102	Mean	SD	t	Sig. (2-tailed)
CVLT correct (%)	**0.49**	**0.14**	**19.15****	**<.001**
ERLT correct (%)	**0.28**	**0.11**		
CVLT perseverations	**4.02**	**3.97**	**2.55***	**.012**
ERLT perseverations	**2.99**	**3.02**		
CVLT intrusions	**1.52**	**2.23**	**-6.62****	**<.001**
ERLT intrusions	**3.61**	**2.83**		

(*p<0.05, **p<0.01)

II.4.2.2) NART and ERLT

Correlations between the NART and the Experimental Recall semantic categories are shown in Table II.4.2.2.

TABLE II.4.2.2) CORRELATIONS BETWEEN EXPERIMENTAL RECALL VERBAL LEARNING TASK AND NART ERROR SCORE

N=98		NART
Correct	Pearson corr.	**-.422****
	Sig. (2-tailed)	**<.001**
Perseverations	Pearson corr.	-.194
	Sig. (2-tailed)	.055
Intrusions	Pearson corr.	-.006
	Sig. (2-tailed)	.955
Neutral	Pearson corr.	**-.213***
	Sig. (2-tailed)	**.035**
Sensory	Pearson corr.	-.182
	Sig. (2-tailed)	.073
Affective	Pearson corr.	**-.305****
	Sig. (2-tailed)	**.002**
MS	Pearson corr.	**-.237***
	Sig. (2-tailed)	**.019**

(*p<0.05, **p<0.01)

II.4.2.3) CVLT by Hayling Sentence Completion

Correlations between CVLT correct recall and the Hayling Sentence Completion Task Times and Errors are shown in Table II.4.2.3.

TABLE II.4.2.3) CORRELATIONS BETWEEN HAYLING SENTENCE COMPLETION TIMES AND ERRORS AND CVLT CORRECT RECALL SCORE

N=102		CVLT correct recall
Sensible time pain	Pearson corr. Sig. (2-tailed)	**-.368**** **<.001**
Sensible time Non-pain	Pearson corr. Sig. (2-tailed)	**-.319**** **.001**
Non-sensible time pain	Pearson corr. Sig. (2-tailed)	**-.251*** **.001**
Non-sensible Time non-pain	Pearson corr. Sig. (2-tailed)	**-.359**** **<.001**
Pain error	Pearson corr. Sig. (2-tailed)	**-.304**** **.002**
Non-pain error	Pearson corr. Sig. (2-tailed)	**-.369**** **<.001**
Type A error pain	Pearson corr. Sig. (2-tailed)	**-.363**** **<.001**
Type A error non-pain	Pearson corr. Sig. (2-tailed)	**-.316**** **.001**
Type B error pain	Pearson corr. Sig. (2-tailed)	.092 .357
Type B error non-pain	Pearson corr. Sig. (2-tailed)	-.235 .017

(*p<0.05, **p<0.01)

II.4.2.4) NART by Hayling Sentence Completion

Correlations between NART error score and the Hayling Sentence Completion Task Times and Errors are shown in table II.4.2.4.

TABLE II.4.2.4) CORRELATIONS BETWEEN HAYLING SENTENCE COMPLETION TIMES AND ERRORS AND NART ERROR SCORE

N=98		NART error score
Sensible time pain	Pearson corr.	**.300****
	Sig. (2-tailed)	**.003**
Sensible time Non-pain	Pearson corr.	**.328****
	Sig. (2-tailed)	**.001**
Non-sensible time pain	Pearson corr.	.130
	Sig. (2-tailed)	.203
Non-sensible Time non-pain	Pearson corr.	.177
	Sig. (2-tailed)	.081
Pain error	Pearson corr.	.119
	Sig. (2-tailed)	.244
Non-pain error	Pearson corr.	**.328****
	Sig. (2-tailed)	**.001**
Type A error pain	Pearson corr.	.152
	Sig. (2-tailed)	.136
Type A error non-pain	Pearson corr.	**.299****
	Sig. (2-tailed)	**.003**
Type B error pain	Pearson corr.	-.057
	Sig. (2-tailed)	.576
Type B error non-pain	Pearson corr.	.184
	Sig. (2-tailed)	.070

(*p<0.05, **p<0.01)

II.4.3) SUBJECTIVE VARIABLES

II.4.3.1) SD across subscales and with other measures

Emotional and Disease subscales of the SD are significantly correlated. We would expect these two scales to be correlated as they reflect overall MS impact, as shown in Table II.4.3.1.A.

The subscales of the CMDI were correlated with most of the specific questions of the Emotion and Disease portions of the SD, as shown in Table II.4.3.1.B. This is as expected as these two scales are designed to detect

negative emotional state. The McGill score was significantly correlated with the Pain question of the SD, as shown in Table II.4.3.1.C.

This supports the validity of these measures in the current sample and demonstrates the reliability of self-report with regard to mood and subjective pain measures.

TABLE II.4.3.1.A) CORRELATIONS BETWEEN SUBSCALES OF THE SD

N=102		Disease SD
Emotional SD	Pearson corr.	**.485****
	Sig. (2-tailed)	**<.001**

(*p<0.05, **p<0.01)

TABLE II.4.3.1.B) CORRELATIONS BETWEEN THE CMDI AND SPECIFIC QUESTIONS IN DISEASE SD

		Ill	Disabled	In pain	Fatigued
Mood	Pearson corr.	**.349****	**.246***	**.342****	**.284****
CMDI	Sig. (2-tailed)	**<.001**	**.013**	**<.001**	**.004**
Evaluative	Pearson corr.	**.253***	.178	**.323****	**.246***
CMDI	Sig. (2-tailed)	**.010**	.074	**.001**	**.013**
Vegetative	Pearson corr.	**.326****	**.261****	**.348****	**.428****
CMDI	Sig. (2-tailed)	**.001**	**.008**	**<.001**	**<.001**
Total CMDI	Pearson corr.	**.356****	**.261****	**.387****	**.360****
	Sig. (2-tailed)	**<.001**	**.008**	**<.001**	**<.001**

(*p<0.05, **p<0.01)

TABLE II.4.3.1.C) MCGILL SCORE AND SD FOR PAIN

		In pain
Total McGill Score (intensity)	Pearson corr. Sig. (2-tailed)	**.447**** **<.001**
Total McGill Adjectives (Specific descriptors)	Pearson corr. Sig. (2-tailed)	**.426**** **<.001**

(*p<0.05, **p<0.01)

II.4.3.2) PD subscales

The Pain PD and the Discomfort PD scales are similar in format and some much of the information may be the same so means testing was completed to look for differences between the two scales, as shown in Table II.4.3.2. The only significant difference between items on the Pain PD and Discomfort PD scales was with 'My pain/discomfort does not stop me from enjoying life' with the mean of those with "Discomfort" saying discomfort interfered with their enjoyment more significantly than for those with "Pain" as shown in Table II.4.3.2. This may be due to those with high discomfort experiencing more negative emotional effects and less enjoyment overall. Alternatively, it may be that high Pain comes more in bursts and may be of overall shorter duration than high Discomfort, leading to discomfort having an overall larger impact on enjoyment in daily life.

TABLE II.4.3.2) PAIN AND DISCOMFORT PD MEANS

N=102	Mean	SD	t	Sig. (2-tailed)
Total pain	12.23	8.22	0.55	.586
Total discomfort	12.48	8.50		
Scared about my pain	1.13	1.23	0.84	.836
Scared about discomfort	1.15	1.25		
My pain is unbearable	1.19	1.32	1.57	.121
My discomfort is unbearable	1.03	1.17		
My pain is torturing me	0.97	1.27	1.46	.255
My discomfort is torturing me	0.85	1.16		
My pain stops me from enjoying life	1.11	1.28	**-2.23***	**.028**
My discomfort stops me from enjoying life	1.34	1.42		
I cannot tolerate my pain	0.94	1.14	-0.67	.505
I cannot tolerate my discomfort	1.02	1.15		
I feel helpless about my pain	1.67	1.48	-0.60	.552
I feel helpless about my discomfort	1.74	1.43		
My pain is not just a minor annoyance	1.46	1.34	-1.43	.156
My discomfort is not just a minor annoyance	1.64	1.33		
I am distressed about my pain	1.25	1.26	0.16	.874
I am distressed about my discomfort	1.24	1.34		
My pain affects my outlook on life	1.23	1.38	-0.39	.699
My discomfort affects my outlook on life	1.27	1.38		
I am a different person when I have pain	1.28	1.37	0.75	.452
I am a different person when I have disc.	1.21	1.29		

(*p<0.05, **p<0.01)

II.4.3.3) SOPA across subscales and with other measures

Correlation between SOPA subscales is shown in Table II.4.3.3.A. The correlations within the scales and between the two scales may better enable the classification of adaptive or non-adaptive coping mechanisms. The links are mainly between coping strategies and the belief of being disabled by their pain, suggesting that different levels of perceived disability may dictate specific coping styles.

TABLE II.4.3.3.A) CORRELATIONS BETWEEN SOPA SUBSCALES

N=84		Control	Disabling	Harm	Emotion	Medication	Solicitude	Medical cure
Control	Pearson corr							
	Sig. (2-tailed)							
Disabling	Pearson corr	-.184						
	Sig. (2-tailed)	.093						
Harm	Pearson corr	.012	**.423****					
	Sig. (2-tailed)	.913	**<.001**					
Emotion	Pearson corr	**.324****	.157	-.024				
	Sig. (2-tailed)	**.003**	.155	.828				
Medication	Pearson corr	-.146	**.366****	.191	-.019			
	Sig. (2-tailed)	.186	**.001**	.081	.860			
Solicitude	Pearson corr	.109	.177	.021	**.495****	.151		
	Sig. (2-tailed)	.324	.108	.849	**<.001**	.170		
Medical	Pearson corr	**.318****	.140	.002	.197	**.372****	**.350****	
Cure	Sig. (2-tailed)	**.003**	.203	.988	.072	**<.001**	**.001**	

(*p<0.05, **p<0.01)

TABLE II.4.3.3.B) CORRELATIONS BETWEEN SOPA AND CMSS SUBSCALE (*P<0.05, **P<0.01)

	SOPA	Control	Disability	Harm	Emotion	Medication	Solicitude	Medical cure
CMSS								
Acceptance	Pearson corr.	.075	-.147	-.083	-.072	**.226***	.053	.156
	Sig. (2-tailed)	.496	.182	.452	.518	**.038**	.638	.632
Social	Pearson corr.	.012	-.030	-.205	.191	.090	.064	.142
support	Sig. (2-tailed)	.913	.788	.062	.082	.415	.564	.199
Energy	Pearson corr.	.024	**.247***	**.307****	-.090	.163	-.061	.063
conservation	Sig. (2-tailed)	.830	**.024**	**.005**	.414	.139	.581	.569
Emotional	Pearson corr.	.001	-.102	.045	.120	.150	.137	.214
release	Sig. (2-tailed)	.991	.357	.684	.275	.172	.212	.051
Problem	Pearson corr.	.116	**-.225***	-.074	-.101	**.252***	-.118	.088
solving	Sig. (2-tailed)	.293	**.040**	.504	.359	**.021**	.287	.428
Physical	Pearson corr.	-.104	**.229***	.119	-.009	**.307***	.049	.046
assistance	Sig. (2-tailed)	.348	**.037**	.282	.936	**.005**	.656	.678
Avoidance	Pearson corr.	.091	**-.271***	.065	-.098	.070	.038	-.020
	Sig. (2-tailed)	.413	**.013**	.558	.377	.529	.733	.859
Personal	Pearson corr.	-.053	-.154	**-.242***	.035	.139	.110	.167
health ctrl	Sig. (2-tailed)	.633	.161	**.027**	.754	.206	.318	.130

II.4.4) COGNITIVE ASSESSMENT

The CVLT by MS subtype did not show any significant differences when compared (t-test). Some studies have found the level of cognitive impairment to be more severe in SP MS than in PP MS (Comi et al., 1995) but not all (Foong et al., 2000). Performance may also vary by type of assessment used or area of deficit explored. The comparability of the two MS subtypes, both in terms of pre-morbid level and current memory function makes it unlikely that any differences between the two subtypes could be mediated by different current intellectual ability.

II.4.5) EMOTION SCALES

II.4.5.1) HADS Depression and Anxiety and CMDI

Depression and anxiety are significantly correlated with all subscales of the CMDI, as shown in Table II.4.5.2. The association between HADS depression and CMDI is reasonable as both scales are designed to detect depression status. In addition, as anxiety is usually correlated with depression, the correlation between HADS anxiety and CMDI is not surprising. This supports the validity of these measures in the current sample and demonstrates the reliability of their self-report on mood measures.

II.4.5.2) SD and CMDI

The Emotional SD and Disease SD are significantly correlated with all subscales and the Total CMDI, as shown in Table II.4.5.2.A. It is expected that the CMDI and the Emotion SD would be correlated as both are measuring emotional status, as shown in Table II.4.5.2.B. The correlation between Disease SD and the CMDI is more interesting as it illustrates the relationship between physical disease state and emotional factors.

TABLE II.4.5.2.A) CORRELATIONS BETWEEN CMDI AND HADS

		Depression HADS	Anxiety HADS
Mood CMDI	Pearson corr.	**.661****	**.664****
	Sig. (2-tailed)	**<.001**	**<.001**
Evaluative CMDI	Pearson corr.	**.612****	**.616****
	Sig. (2-tailed)	**<.001**	**<.001**
Vegetative CMDI	Pearson corr.	**.529****	**.546****
	Sig. (2-tailed)	**<.001**	**<.001**
Total CMDI	Pearson corr.	**.694****	**.703****
	Sig. (2-tailed)	**<.001**	**<.001**

(*p<0.05, **p<0.01)

TABLE II.4.5.2.B) CORRELATIONS BETWEEN CMDI AND TWO SUBSCALES OF THE SD

		Total emotional SD	Total disease SD
Mood CMDI	Pearson corr.	**.604****	**.446****
	Sig. (2-tailed)	**<.001**	**<.001**
Evaluative CMDI	Pearson corr.	**.539****	**.355****
	Sig. (2-tailed)	**<.001**	**<.001**
Vegetative CMDI	Pearson corr.	**.396****	**.510****
	Sig. (2-tailed)	**<.001**	**<.001**
Total CMDI	Pearson corr.	**.597****	**.498****
	Sig. (2-tailed)	**<.001**	**<.001**

(*p<0.05, **p<0.01)

II.4.6) IMPACT FACTORS

II.4.6.1) MSIS

The means of the subscales of the MSIS were significantly correlated with each other and with the total score, as shown in Table II.4.6.1. This may not be surprising as impact in either domain is likely to have some effect on impact in the alternative domain.

TABLE II.4.6.1) SUBSCALES OF THE MSIS

		Emotional	Total
Physical	Pearson corr.	**.542****	**.952****
	Sig. (2-tailed)	**<.001**	**<.001**
Total	Pearson corr.	**.773****	
	Sig. (2-tailed)	**<.001**	

(*p<0.05, **p<0.01)

II.4.6.2) FIS

The subscales of the FIS were significantly correlated with each other and with the total. This fits with clinical experience of fatigue as a wide-ranging problem likely to impact in more than one domain.

TABLE II.4.6.2) SUBSCALES OF FIS

		Social	Total
Cognitive	Pearson corr.	**.802****	**.877****
	Sig. (2-tailed)	**<.001**	**<.001**
Physical	Pearson corr.	**.824****	**.879****
	Sig. (2-tailed)	**<.001**	**<.001**
Total	Pearson corr.	**.976****	
	Sig. (2-tailed)	**<.001**	

(*p<0.05, **p<0.01)

II.4.6.3) CMSS

Correlations between the different CMSS subscales are given in Table II.4.6.3. These intercorrelations are similar to previous findings (Pakenham, 2001) in that the many of the subscales were significantly correlated.

TABLE II.4.6.3) CMSS SUBSCALE CORRELATIONS

N=102		Accept-ance	Social Support	Energy Conserv.	Emotional release	Problem solving	Physical assistance	Avoid-ance	Personal Health Ctrl.
Acceptance	Pearson Cr Sig.								
Social support	Pearson Cr Sig.	.106 .287							
Energy conserv.	Pearson Cr Sig.	.052 .602	.124 .215						
Emotional release	Pearson Cr Sig.	**.290**** **.003**	**.423**** **<.001**	**.373**** **<.001**					
Problem solving	Pearson Cr Sig.	**.347**** **<.001**	**.085** **.395**	**.375**** **<.001**	**.517**** **<.001**				
Physical assistance	Pearson Cr Sig.	**.261**** **.008**	**.103** **.302**	**.239**** **.016**	**.259**** **.009**	**.323**** **.001**			
Avoidance	Pearson Cr Sig.	**.378**** **<.001**	-.167 .094	-.098 .325	.055 .582	**.201**** **.043**	.080 .426		
Personal Health Ctrl.	Pearson Cr Sig.	.152 .128	**.319**** **.001**	.068 .497	**.392**** **<.001**	**.330**** **.001**	.176 .077	-.053 .599	

(*p<0.05, **p<0.01)

TABLE III.1.1.1.1.B) FREQUENCY OF MCGILL ADJECTIVES FOR HIGH 'COMFORTABLE' VS. 'IN PAIN' SD (2,3 OR 4) (N=59) (1ST PART)*

N=59	Frequency	Percent		Frequency	Percent
Flickering	1	1.7	Quivering	7	11.9
Pulsing	4	6.8	**Throbbing**	25	42.4
Beating	1	1.7	Pounding	3	5.1
Jumping	13	22.0	Flashing	3	5.1
Shooting	13	22.0	Pricking	10	16.9
Boring	8	13.6	Drilling	1	1.7
Stabbing	10	16.9	Lancinating	0	0.0
Sharp	19	32.2	Cutting	3	5.1
Lacerating	1	1.7	Pinching	3	5.1
Pressing	3	5.1	Gnawing	9	15.3
Cramping	24	40.7	Crushing	5	8.5
Tugging	6	10.2	Pulling	5	8.5
Wrenching	8	13.6	Hot	10	16.9
Burning	16	27.1	Scalding	1	1.7
Searing	5	8.5	***Tingling***	17	28.8
Itchy	10	16.9	Smarting	2	3.4
Stinging	8	13.6	Dull	6	10.2
Sore	3	5.1	Hurting	4	6.8
Aching	14	23.7	***Heavy***	27	45.8
Tender	12	20.3	Taut	14	23.7

*Comparisons of the ten most commonly endorsed words for each of the two SD score groups are in italic text for same words and in bold text for those that are different.

TABLE III.1.1.1.1.C) FREQUENCY OF MCGILL ADJECTIVES FOR LOW 'COMFORTABLE' VS. 'IN PAIN' SD (0 OR 1) (N=43) (2ND PART)*

N=43	Frequency	Percent		Frequency	Percent
Rasping	0	0.0	Splitting	4	9.3
Tiring	12	27.9	***Exhausting***	20	46.5
Sickening	7	16.3	Suffocating	3	7.0
Fearful	9	20.9	Frightful	1	2.3
Terrifying	3	7.0	Punishing	5	11.6
Gruelling	3	7.0	Cruel	1	2.3
Vicious	2	4.7	Killing	1	2.3
Wretched	4	9.3	Blinding	2	4.7
Annoying	14	32.6	Troublesome	1	2.3
Miserable	3	7.0	Intense	6	14.0
Unbearable	4	9.3	Spreading	2	4.7
Radiating	6	14.0	Penetrating	2	4.7
Piercing	2	4.7	Tight	3	7.0
Numb	16	37.2	Drawing	0	0.0
Squeezing	2	4.7	Tearing	2	4.7
Cool	6	14.0	Cold	8	18.6
Freezing	4	9.3	***Nagging***	11	25.6
Nauseating	2	4.7	Agonising	3	7.0
Dreadful	2	4.7	Torturing	3	7.0

*Comparisons of the ten most commonly endorsed words for each of the two SD score groups are in italic text for same words and in bold text for those that are different.

TABLE III.1.1.1.1.D) FREQUENCY OF MCGILL ADJECTIVES FOR HIGH 'COMFORTABLE' VS. 'IN PAIN' SD (2,3 OR 4) (N=59) (2ND PART)*

N=59	Frequency	Percent		Frequency	Percent
Rasping	0	0.0	Splitting	5	8.5
Tiring	25	42.4	***Exhausting***	24	40.7
Sickening	7	11.9	Suffocating	5	8.5
Fearful	6	10.2	Frightful	4	6.8
Terrifying	5	8.5	Punishing	9	15.3
Gruelling	9	15.3	Cruel	3	5.1
Vicious	2	3.4	Killing	2	3.4
Wretched	12	20.3	Blinding	2	3.4
Annoying	14	23.7	Troublesome	14	23.7
Miserable	9	15.3	Intense	9	15.3
Unbearable	7	11.9	Spreading	7	11.9
Radiating	6	10.2	Penetrating	8	13.6
Piercing	8	13.6	Tight	10	16.9
Numb	20	33.9	Drawing	2	3.4
Squeezing	4	6.8	Tearing	2	3.4
Cool	6	10.2	**Cold**	16	27.1
Freezing	6	10.2	***Nagging***	21	35.6
Nauseating	4	6.8	Agonising	6	10.2
Dreadful	2	3.4	Torturing	8	13.6

*Comparisons of the ten most commonly endorsed words for each of the two SD score groups are in italic text for same words and in bold text for those that are different.

III.1.1.2) McGill adjectives by McGill group (high/low)

Tests on the parametric assumptions of the variable were completed to test for normality of the data and equality of the variance. Tests of skew (skewness/standard error of the skew was <2.58) showed that there was not significant skew at the $p<0.01$ level. Tests of kurtosis (kurtosis/standard error of the kurtosis was <2.58) showed that there was not significant kurtosis at the $p<0.01$ level. The results of Levene's test were not significant, indicating that the assumption of equal variances was reasonable. Following these tests of assumptions, means for the McGill intensity score and McGill adjectives by McGill intensity group (high/low) are given in Table III.1.1.2.A.

TABLE III.1.1.2) T-TEST RESULTS FOR DIFFERENCES IN MEAN LEVEL OF PAIN ADJECTIVES BETWEEN HIGH AND LOW PAIN GROUPS

	McGill group	N	Mean	SD	t	Sig. (2-tailed)
Total McGill adjectives	High	49	**33.04**	**7.98**	**-14.02***	**<.001**
	Low	53	**12.55**	**6.78**		

*p<0.01

III.1.1.2.1 McGill group (high/low) by most common McGill adjectives

Comparisons of the ten most commonly endorsed words for each of the two McGill intensity score groups are in italic text for same words and in bold text for those that are different for added clarification, also as shown in Tables III.1.1.2.1.A-D. There were differences between the words chosen by the high McGill versus low McGill intensity groups; however the overall finding was that there was a larger overlap in the words chosen than there were differences between them. Therefore, the hypothesis was not supported, patients reporting 'pain' when questioned did not select a different pattern of adjectives from the McGill to describe qualitative aspects of their pain, than those not reporting 'pain'.

For those with a low McGill pain intensity score (N=53), the most commonly endorsed words were *TIRING* (20, 38%), **ANNOYING** (20, 38%), **TINGLING** (17,32%), *CRAMPING* (16, 30%), *NUMB* (16, 30%), *NAGGING* (15, 28%), *HEAVY* (15, 28%), *EXHAUSTING* (15, 28%), **ACHING** (13, 25%), *THROBBING* (11, 21%).

For those with a high McGill pain intensity score (N=49), the most commonly endorsed words were *EXHAUSTING* (29, 59%), *HEAVY* (22, 45%), *CRAMPING* (21, 43%), **SHOOTING** (20, 41%), *THROBBING* (20, 41%), *NUMB* (20, 41%) *NAGGING* (17, 35%), *TIRING* (17, 35%), **SHARP** (17, 35%), **TAUT** (16, 33%). There is a substantial overlap between the words chosen by the high McGill pain intensity group and the low McGill pain intensity group.

TABLE III.1.1.2.1.A) FREQUENCY OF MCGILL ADJECTIVES FOR LOW MCGILL TOTAL SCORE (0-22) (N=53) (1ST PART)*

N=53	Frequency	Percent		Frequency	Percent
Flickering	4	7.5	Quivering	3	5.7
Pulsing	3	5.7	***Throbbing***	11	20.8
Beating	1	1.9	Pounding	0	0.0
Jumping	8	15.1	Flashing	3	5.7
Shooting	3	5.7	Pricking	8	15.1
Boring	3	5.7	Drilling	1	1.9
Stabbing	3	5.7	Lancinating	1	1.9
Sharp	5	9.4	Cutting	0	0.0
Lacerating	0	0.0	Pinching	1	1.9
Pressing	4	7.5	Gnawing	3	5.7
Cramping	16	30.2	Crushing	1	1.9
Tugging	2	3.8	Pulling	1	1.9
Wrenching	1	1.9	Hot	5	9.4
Burning	6	11.3	Scalding	0	0.0
Searing	1	1.9	**Tingling**	17	32.1
Itchy	8	15.1	Smarting	0	0.0
Stinging	1	1.9	Dull	6	11.3
Sore	2	3.8	Hurting	1	1.9
Aching	13	24.5	***Heavy***	15	28.3
Tender	4	7.5	Taut	5	9.4

*Comparisons of the ten most commonly endorsed words for each of the two McGill intensity score groups are in italic text for same words and in bold text for those that are different.

TABLE III.1.1.2.1.B) FREQUENCY OF MCGILL ADJECTIVES FOR HIGH MCGILL TOTAL SCORE (23 OR GREATER) (N=49) (1ST PART)*

N=49	Frequency	Percent		Frequency	Percent
Flickering	3	6.1	Quivering	7	14.3
Pulsing	5	10.2	***Throbbing***	20	40.8
Beating	0	0.0	Pounding	4	8.2
Jumping	10	20.4	Flashing	1	2.0
Shooting	20	40.8	Pricking	9	18.4
Boring	9	18.4	Drilling	0	0.0
Stabbing	9	18.4	Lancinating	0	0.0
Sharp	17	34.7	Cutting	6	12.2
Lacerating	2	4.1	Pinching	4	8.2
Pressing	3	6.1	Gnawing	8	16.3
Cramping	21	42.9	Crushing	6	12.2
Tugging	6	12.2	Pulling	5	10.2
Wrenching	9	18.4	Hot	14	28.6
Burning	13	26.5	Scalding	2	4.1
Searing	5	10.2	Tingling	10	20.4
Itchy	9	18.4	Smarting	4	8.2
Stinging	11	22.4	Dull	4	8.2
Sore	4	8.2	Hurting	5	10.2
Aching	11	22.4	***Heavy***	22	44.9
Tender	15	30.6	**Taut**	16	32.7

*Comparisons of the ten most commonly endorsed words for each of the two McGill intensity score groups are in italic text for same words and in bold text for those that are different.

TABLE III.1.1.2.1.C) FREQUENCY OF MCGILL ADJECTIVES FOR LOW MCGILL TOTAL SCORE (0-22) (N=53) (2ND PART)*

N=53	Frequency	Percent		Frequency	Percent
Rasping	0	0.0	Splitting	2	3.8
Tiring	20	37.7	***Exhausting***	15	28.3
Sickening	3	5.7	Suffocating	0	0.0
Fearful	2	3.8	Frightful	2	3.8
Terrifying	2	3.8	Punishing	2	3.8
Gruelling	5	9.4	Cruel	1	1.9
Vicious	0	0.0	Killing	0	0.0
Wretched	3	5.7	Blinding	0	0.0
Annoying	20	37.7	Troublesome	10	18.9
Miserable	5	9.4	Intense	1	1.9
Unbearable	0	0.0	Spreading	2	3.8
Radiating	4	7.5	Penetrating	1	1.9
Piercing	0	0.0	Tight	5	9.4
Numb	16	30.2	Drawing	1	1.9
Squeezing	1	1.9	Tearing	1	1.9
Cool	5	9.4	Cold	11	20.8
Freezing	3	5.7	***Nagging***	15	28.3
Nauseating	1	1.9	Agonising	2	3.8
Dreadful	2	3.8	Torturing	0	0.0

*Comparisons of the ten most commonly endorsed words for each of the two McGill intensity score groups are in italic text for same words and in bold text for those that are different.

TABLE III.1.1.2.1.D) FREQUENCY OF MCGILL ADJECTIVES FOR HIGH MCGILL TOTAL SCORE (23 OR GREATER) (N=49) (2ND PART)*

N=49	Frequency	Percent		Frequency	Percent
Rasping	0	0.0	Splitting	7	14.3
Tiring	17	34.7	***Exhausting***	29	59.2
Sickening	11	22.4	Suffocating	8	16.3
Fearful	13	26.5	Frightful	3	6.1
Terrifying	6	12.2	Punishing	12	24.5
Gruelling	7	14.3	Cruel	3	6.1
Vicious	4	8.2	Killing	3	6.1
Wretched	13	26.5	Blinding	4	8.2
Annoying	8	16.3	Troublesome	5	10.2
Miserable	7	14.3	Intense	14	28.6
Unbearable	11	22.4	Spreading	7	14.3
Radiating	8	16.3	Penetrating	9	18.4
Piercing	10	20.4	Tight	8	16.3
Numb	20	40.8	Drawing	1	2.0
Squeezing	5	10.2	Tearing	3	6.1
Cool	7	14.3	Cold	13	26.5
Freezing	7	14.3	***Nagging***	17	34.7
Nauseating	5	10.2	Agonising	7	14.3
Dreadful	2	4.1	Torturing	11	22.4

*Comparisons of the ten most commonly endorsed words for each of the two McGill intensity score groups are in italic text for same words and in bold text for those that are different.

III.1.2) PSYCHOLOGICAL FACTORS with TOTAL McGill SCORE – HYPOTHESIS 2

Pain is known to be linked to distress in many conditions. However, MS carries an increased risk of psychiatric morbidity with or without pain. Therefore, emotional distress links to pain in MS are likely to be complex.

The hypothesis is derived from the argument that although pain is significantly linked to depression in most populations (Clark et al., 2000), anxiety may be more significant in the MS population due to pain-related fear (Hadjistavropoulos et al., 2004). This is theorized to occur because as MS is so unpredictable (McDonald and Ron, 1999) perhaps pain may act as a signal that the individual may be getting worse or having a relapse and perhaps may interact with a propensity toward mood disorders. If this is the case, this would be more true for SP than for PP (Vleugels et al., 1998; McDonald and Ron, 1999).

Hypothesis 2.1

Patients with more pain will have higher anxiety and depression. Precisely when the patient population is split into high and low McGill intensity score, the high McGill intensity score group will have higher anxiety scores on the HADS and higher depression on the HADS and CMDI.

There was a significant difference in HADS anxiety score for those with a McGill intensity high score versus a low score. There were significant differences in HADS anxiety item means for high versus low McGill intensity score for items: frightened and restless. There were no differences for HADS depression overall score or item scores for those with a high versus a low McGill intensity score.

There were no differences for CMDI overall score or subscale scores for those with a high versus a low McGill intensity score.

The hypothesis was supported for anxiety but not depression. Those patients with more pain had higher anxiety but not significantly more or less depression. Details by measure will follow in Sections III.1-2.

Hypothesis 2.2

Patients with more pain will have more illness intrusiveness. Precisely when the patient population is split into high and low McGill intensity score, the

high McGill intensity score group will have significantly different pain attitudes and impact of MS than the low McGill intensity score group, as demonstrated by SOPA and MSIS subscale scores.

There were significant differences in pain attitudes for those with high versus low pain, with those with high pain expecting a medical cure for their pain. There were no significant differences for the impact of MS by pain intensity level. The hypothesis was supported: the high McGill intensity score group had significantly different pain attitudes than the low McGill intensity score group. Details by measure will follow in Sections III.3-4.

III.1.2.1) HADS by McGill

Tests on the parametric assumptions of the variable were completed to test for normality of the data and equality of the variance. Certain tests of skew (skewness/standard error of the skew were $\geq$2.58) showed that there was significant skew at the $p<0.01$ level. Certain other tests of kurtosis (kurtosis/standard error of the kurtosis were $\geq$2.58) showed that there was significant kurtosis at the $p<0.01$ level. In cases where the data were skewed and/or showed significant kurtosis, transformation was completed, first using Log transformation and if necessary, square root transformation. The first transformation showing a new variable without skew and kurtosis was used. If neither transformation significantly reduced the skew and/or kurtosis to bring it/them within acceptable levels, the transformation showing the most reduction in skew was used (as the skew is generally considered more of a problem than kurtosis) and a footnote to indicate this is included. Such results should be interpreted with caution. If any of the results of Levene's test were significant, the t-test value corresponding to 'equal variance not assumed' was used and a footnote to indicate this was included.

HADS overall means by McGill intensity group are compared in Table III.1.2.1.A. Means of the HADS depression scale were compared using McGill intensity group (high/low) and these are given in Table III.1.2.1.B. Means of the HADS anxiety questions were compared using McGill intensity group (high/low) and these are given in Table III.1.2.1.C.

The mean scores for the HADS depression questions were not significantly different for the high versus low McGill total scores. The mean score

for the HADS anxiety were significantly different for the high versus low McGill total scores with those with more pain having more anxiety. The mean scores for the HADS anxiety questions: Frightened and Feeling Restless were significantly different for the high versus low McGill total scores with those having higher pain report being more frightened and more restless.

TABLE III.1.2.1.A) T-TEST RESULTS FOR DIFFERENCES IN MEAN SUBSCALE SCORES FOR HADS MOOD SCALES BETWEEN HIGH AND LOW PAIN GROUPS (MCGILL)

N=102	McGill group	N	Mean	SD	t	Sig. (2-tailed)
Total depression	High	49	6.43	4.11	0.73	.465
	Low	53	5.89	3.33		
Total anxiety$^{\surd}$	High	49	**3.03**	**4.71**	**2.86***	**.005**
	Low	53	**2.59**	**4.15**		

*$p<0.01$

$^{\surd}$Square root transformation

TABLE III.1.2.1.B) T-TEST RESULTS FOR DIFFERENCES IN MEAN LEVEL OF ENDORSEMENT OF SPECIFIC ITEMS ON HADS DEPRESSION SCALE BETWEEN HIGH AND LOW PAIN GROUPS.

N=102	McGill High	N	Mean	SD	t	Sig. (2-tailed)
Enjoy	High	49	1.08	.91	-0.07	.942
	Low	53	1.09	.84		
Laugh$^{\pm}$	High	49	0.11	.16	0.298$^{\#}$	.766
	Low	53	0.10	.15		
Cheerless$^{\pm}$	High	49	0.17	.20	0.63$^{\#}$	.530
	Low	53	0.15	.17		
Slowed down$^{\surd}$	High	49	1.80	.24	1.08$^{\#}$	.281
	Low	53	1.74	.30		
Appearance$^{\surd}$	High	49	1.28	.33	-0.45	.655
	Low	53	1.31	.31		
Forward$^{\surd}$	High	49	1.33	.33	.11	.917
	Low	53	1.33	.27		
Book$^{\pm}$	High	49	0.110.45	.20	1.73$^{\wedge,\#}$	.087
	Low	53	0.050.19	.13		

$^{\pm}$Log transformation

$^{\surd}$Square root transformation

$^{\wedge}$Equal variances not assumed

$^{\#}$After transformation statistically significant skewness, kurtosis or both remained

TABLE III.1.2.1.C) T-TEST RESULTS FOR DIFFERENCES IN MEAN LEVEL OF ENDORSEMENT OF SPECIFIC ITEMS ON HADS ANXIETY SCALE BETWEEN HIGH AND LOW PAIN GROUPS (MCGILL)

N=102	McGill group	N	Mean	SD	t	Sig. (2-tailed)
Tense$^{\pm}$	High	49	.30	0.17	.29	.776
	Low	53	.29	0.15		
Frightened$^{\surd}$	High	49	**1.48**	**0.39**	**3.13**$^{*,\#}$	**.002**
	Low	53	**1.255**	**0.35**		
Worry	High	49	1.41	1.08	1.28	.203
	Low	53	1.15	0.95		
Ill at ease	High	49	1.29	0.91	2.12^	.037
	Low	53	0.94	0.69		
Butterflies$^{\surd}$	High	49	1.36	0.29	2.28	.025
	Low	53	1.24	0.27		
Restless	High	49	**1.47**	**0.82**	**2.66***	**.009**
	Low	53	**1.02**	**0.89**		
Panic$^{\surd}$	High	49	1.43	0.33	1.82	.068
	Low	53	1.30	0.31		

*$p<0.01$
$^{\pm}$Log transformation
$^{\surd}$Square root transformation
^equal variances not assumed
#After transformation statistically significant skewness, kurtosis or both remained

III.1.2.2) CMDI by McGill

Tests on the parametric assumptions of the variable were completed to test for normality of the data and equality of the variance. Certain tests of skew (skewness/standard error of the skew were $\geq$2.58) showed that there was significant skew at the $p<0.01$ level. Certain other tests of kurtosis (kurtosis/standard error of the kurtosis were $\geq$2.58) showed that there was significant kurtosis at the $p<0.01$ level. In cases where the data were skewed and/or showed significant kurtosis, transformation was completed, first using Log transformation and if necessary, square root transformation. The first transformation showing a new variable without skew and kurtosis was used. If neither transformation significantly reduced the skew and/or kurtosis to bring it/them within acceptable levels, the one showing the most reduction in skew was used (as the skew is generally considered more of a problem than kurtosis when

it deviates from normality) and a footnote to indicate this is included. Such results should be interpreted with caution. If any of the results of Levene's test were significant, the t-test value corresponding to 'equal variance not assumed' was used and a footnote to indicate this was included. Tests of the difference of the means for the CMDI subscales are shown in Table III.1.2.2. These means are not statistically different.

TABLE III.1.2.2) T-TEST RESULTS FOR DIFFERENCES IN MEANS OF SUBSCALE SCORES FOR CMDI MOOD SCALE BETWEEN HIGH AND LOW PAIN GROUPS (MCGILL)

	McGill	N	Mean	SD	t	Sig. (2-tailed)
Mood[±]	High	49	30.02	14.48	1.50	.132
	Low	53	26.21	11.09		
Evaluative[±]	High	49	25.90	13.37	1.61[#]	.112
	Low	53	22.23	9.11		
Vegetative	High	49	39.98	11.08	1.89	.061
	Low	53	36.21	9.02		
Total[±]	High	49	95.90	33.65	1.91	.059
	Low	53	84.64	25.64		

[±]Log transformation

[#]After transformation statistically significant skew remained

III.1.2.3) SOPA by McGill group (high/low)

Tests on the parametric assumptions of the variable were completed to test for normality of the data and equality of the variance. Tests of skew (skewness/standard error of the skew was <2.58) showed that there was not significant skew at the $p<0.01$ level. Tests of kurtosis (kurtosis/standard error of the kurtosis was <2.58) showed that there was not significant kurtosis at the $p<0.01$ level. The results of Levene's test were not significant, indicating that the assumption of equal variances was reasonable. Following these tests of assumptions, a comparison of these means is shown and the one with a statistically significant difference is shown in Table III.1.2.3. The Medical Cure (SOPA) score was significantly higher in the high McGill group compared to the low McGill group.

TABLE III.1.2.3) SOPA BY MCGILL GROUP (HIGH/LOW)

N=84 (Only given to those reporting some pain)	McGill Hi	N	Mean	SD	t	Sig. (2-tailed)
Control	High	49	18.24	5.89	-0.07	.949
	Low	53	18.33	6.70		
Disability	High	49	20.11	6.92	-0.17	.864
	Low	53	20.38	7.72		
Harm	High	49	15.67	5.41	0.44	.663
	Low	53	15.13	5.89		
Emotion	High	49	14.58	5.81	1.05	.296
	Low	53	13.21	6.15		
Medication	High	49	16.56	4.94	1.80	.076
	Low	53	14.51	5.50		
Solicitude	High	49	10.00	6.22	2.13	.036
	Low	53	7.31	5.22		
Medical Cure	High	49	**18.56**	**5.53**	**3.36***	**.001**
	Low	53	**14.56**	**5.32**		

*$p<0.01$

III.1.2.4) MSIS by McGill

Tests on the parametric assumptions of the variable were completed to test for normality of the data and equality of the variance. Tests of skew (skewness/standard error of the skew was <2.58) showed that there was not significant skew at the $p<0.01$ level. Tests of kurtosis (kurtosis/standard error of the kurtosis was <2.58) showed that there was not significant kurtosis at the $p<0.01$ level. The results of Levene's test were not significant, indicating that the assumption of equal variances was reasonable. Following these tests of assumptions, means for MSIS subscales by McGill intensity groups are given in Table III.1.2.4. These means are not statistically different.

TABLE III.1.2.4) T-TEST RESULTS FOR DIFFERENCES IN MEANS OF MSIS SUBSCALE SCORES BETWEEN HIGH AND LOW PAIN GROUPS (MCGILL)

N=102	McGill	N	Mean	SD	t	Sig. (2-tailed)
PHYSICAL	High	49	68.31	17.61	1.20	.113
	Low	53	62.94	16.30		
EMOTIONAL	High	49	24.45	8.70	0.73	.045
	Low	53	21.19	7.49		
TOTAL OVERALL	High	49	92.76	28.82	1.95	.054
	Low	53	84.13	20.81		

III.2) PAIN VS DISCOMFORT – HYPOTHESIS 3

Patients, clinically evaluated as similar, report their symptoms to be different. Most notably, some report 'pain' while others report 'discomfort'. First, in regard to pain report, it is expected that certain people will have definite pain and term that pain as such. Others will have symptoms that might well objectively be termed pain but subjectively be termed discomfort by them. The effect of the name choice is proposed to have some link to anxiety/depression (distress) (Clark et al., 2000). This link may go in either direction, i.e., those with 'pain' may be more or less likely to be anxious than those who use the term 'discomfort'. This relationship could work in one of two ways: people who use the term 'pain' may have more anxiety/depression due to having a higher intensity of pain (Magni et al., 1994). People who use the term 'discomfort' may have more anxiety/depression due to the inability to communicate their pain/discomfort to others thereby gaining support (Holzberg et al., 1996). In addition, the naming of the pain/discomfort may affect their coping style and pain attitudes as this description may impact their concept of their social support network and self-efficacy (Coughlin et al., 2000). The distribution of high/low Pain PD by high/low Discomfort PD is given in Table III.2.

TABLE III.2) HIGH PAIN/LOW PAIN BY HIGH DISCOMFORT/LOW DISCOMFORT

	High Pain	Low Pain
High Discomfort	40	6
Low Discomfort	5	33

III.2.1) Emotion by PD

Hypothesis 3.1

Those who report higher levels of pain will differ in their distress from those who report higher levels of discomfort. Precisely, means testing will be performed on pain and discomfort PD groups to determine how distress is linked to reported pain and reported discomfort. HADS anxiety and depression and CMDI depression will be tested.

Tests of the differences in means (t-test) were completed on the Pain/Discomfort PD scale: high pain versus low pain and, high discomfort versus low discomfort to determine which groups were significantly different by distress level. The high Pain PD and Discomfort PD group had significantly higher means for HADS Anxiety and HADS Depression. The high Pain PD and Discomfort PD group had significantly higher means for all CMDI subscales. The hypothesis was not supported: Those who report higher levels of pain will differ in their distress from those who report higher levels of discomfort, as both those with high Pain PD and high Discomfort PD experienced high anxiety and high depression. Details by measure will follow in Sections III.2.1.1-2.

III.2.1.1) HADS by PD

Tests on the parametric assumptions of the variable were completed to test for normality of the data and equality of the variance. Certain tests of skew (skewness/standard error of the skew were ≥ 2.58) showed that there was significant skew at the $p<0.01$ level. Certain other tests of kurtosis (kurtosis/standard error of the kurtosis were ≥ 2.58) showed that there was significant kurtosis at the $p<0.01$ level. In cases where the data were skewed and/or showed significant kurtosis, transformation was completed, first using Log transformation and if necessary, square root transformation. The first transformation showing a new variable without skew and kurtosis was used. If neither transformation significantly reduced the skew and/or kurtosis to bring it/them within acceptable levels, the transformation showing the most reduction in

skew was used (as the skew is generally considered more of a problem than kurtosis when it deviates from normality) and a footnote to indicate this is included. Such results should be interpreted with caution. If any of the results of Levene's test were significant, the t-test value corresponding to 'equal variance not assumed' was used and a footnote to indicate this was included.

III.2.1.1.1) Anxiety (HADS) by PD

Means of Anxiety (HADS) by Pain PD group are given in Table III.2.1.1.1.A. The Anxiety (HADS) score is significantly higher in the high Pain PD group compared to the low Pain PD group. Means of Anxiety (HADS) by Discomfort PD group are given in Table III.2.1.1.1.B. The Anxiety (HADS) score is significantly higher in the high Discomfort PD group compared to the low Discomfort PD group.

TABLE III.2.1.1.1.A) T-TEST RESULTS FOR DIFFERENCES IN MEANS OF HADS ANXIETY SUBSCALE SCORE BETWEEN HIGH AND LOW PAIN GROUPS (PD)

N=102	Pain (PD) group	N	Mean	SD	t	Sig. (2-tailed)
Anxiety (HADS)$^{\surd}$	High	48	**3.17**	**.72**	**4.82***	**<.001**
	Low	54	**2.48**	**.72**		

*p<0.01

$^{\surd}$Square root transformation

TABLE III.2.1.1.1.B) T-TEST RESULTS FOR DIFFERENCES IN MEANS OF HADS ANXIETY SUBSCALE SCORE BETWEEN HIGH AND LOW DISCOMFORT GROUPS (PD)

N=102	Discomfort (PD) group	N	Mean	SD	t	Sig. (2-tailed)
Anxiety (HADS)$^{\sqrt{}}$	High	50	**3.19**	**.68**	**5.50***	**<.001**
	Low	52	**2.43**	**.72**		

*p<0.01

$^{\sqrt{}}$Square root transformation

III.2.1.1.2) Depression BY PD

Means of Depression (HADS) by Pain PD group are given in Table III.2.1.1.2.A. The Depression (HADS) score is significantly higher in the high pain PD group compared to the low Pain PD group. Means of Depression (HADS) by Discomfort PD group are given in Table III.2.1.1.2.B. The Depression (HADS) score is significantly higher in the high Discomfort PD group compared to the low Discomfort PD group.

TABLE III.2.1.1.2.A) T-TEST RESULTS FOR DIFFERENCES IN MEANS OF HADS DEPRESSION SUBSCALE SCORE BETWEEN HIGH AND LOW PAIN GROUPS (PD)

N=102	Pain (PD) group	N	Mean	SD	t	Sig. (2-tailed)
Depression (HADS)	High	48	**7.58**	**3.65**	**3.39***	**<.001**
	Low	54	**4.87**	**3.32**		

*p<0.01

TABLE III.2.1.1.2.B) T-TEST RESULTS FOR DIFFERENCES IN MEANS OF HADS DEPRESSION SUBSCALE SCORE BETWEEN HIGH AND LOW DISCOMFORT GROUPS (PD)

N=102	Discomfort (PD) group	N	Mean	SD	t	Sig. (2-tailed)
Depression (HADS)	High	50	**7.74**	**3.46**	**4.656***	**<.001**
	Low	52	**4.62**	**3.32**		

*p<0.01

III.2.1.1.3) OVERALL (HADS) MEANS BY PD

Means of Overall HADS by Pain PD group are given in Table III.2.1.1.3.A. The purpose of describing both anxiety and depression together is to address whether there is something significant about the complex of anxiety and depression in determining distress. The Overall HADS score is significantly

higher in the high Pain PD group compared to the low Pain PD group. Means of Overall HADS by Discomfort PD group are given in Table III.2.1.1.3.B. The Overall HADS score is significantly higher in the high Discomfort PD group compared to the low Discomfort PD group.

TABLE III.2.1.1.3.A) T-TEST RESULTS FOR DIFFERENCES IN MEANS OF HADS OVERALL SCORE BETWEEN HIGH AND LOW PAIN GROUPS (PD)

N=102	Pain (PD) group	N	Mean	SD	t	Sig. (2-tailed)
Overall (HADS)	High	48	**17.13**	**7.31**	**4.94***	**<.001**
	Low	54	**10.52**	**6.21**		

*p<0.01

TABLE III.2.1.1.3.B) T-TEST RESULTS FOR DIFFERENCES IN MEANS OF HADS OVERALL SCORE BETWEEN HIGH AND LOW DISCOMFORT GROUPS (PD)

N=102	Discomfort (PD) group	N	Mean	SD	t	Sig. (2-tailed)
Overall (HADS)	High	50	**17.38**	**6.76**	**5.68***	**<.001**
	Low	52	**10.02**	**6.34**		

*p<0.01

III.2.1.2) CMDI by PD

Tests on the parametric assumptions of the variable were completed to test for normality of the data and equality of the variance. Certain tests of skew (skewness/standard error of the skew were $\geq$2.58) showed that there was significant skew at the p<0.01 level. Certain other tests of kurtosis (kurtosis/standard error of the kurtosis were $\geq$2.58) showed that there was significant kurtosis at the p<0.01 level. In cases where the data were skewed and/or showed significant kurtosis, transformation was completed, first using Log transformation and if necessary, square root transformation. The first transformation showing a new variable without skew and kurtosis was used. If neither transformation significantly reduced the skew and/or kurtosis to bring it/them within acceptable levels, the transformation showing the most reduction in skew was used (as the skew is generally considered more of a problem than kurtosis when it deviates from normality) and a footnote to indicate this is included. Such results should be interpreted with caution. If any of the results of Levene's test were significant, the t-test value corresponding to 'equal variance not assumed' was used and a footnote to indicate this was included.

III.2.1.2.1) CMDI subscale means by Pain PD High

Means of CMDI subscales by Pain PD group are given in Table III.2.1.2.1. The Mood, Evaluative, Vegetative and Total CMDI scores are significantly higher in the high Pain PD group compared to the low Pain PD group.

TABLE III.2.1.2.1) T-TEST RESULTS FOR DIFFERENCES IN MEANS OF CMDI SUBSCALE SCORES BETWEEN HIGH AND LOW PAIN GROUPS (PD)

N=102	Pain (PD) group	N	Mean	SD	t	Sig. (2-tailed)
Mood±	High	48	**1.47**	**.19**	**3.40***	**.001**
	Low	54	**1.35**	**.17**		
Evaluative±	High	48	**1.41**	**.18**	**3.68*,#**	**<.001**
	Low	54	**1.28**	**.16**		
Vegetative	High	48	**40.98**	**10.76**	**2.86***	**.005**
	Low	54	**35.39**	**8.95**		
Total±	High	48	**1.99**	**.13**	**3.84***	**<.001**
	Low	54	**1.89**	**.13**		

*p<0.01

±Log transformation

#After transformation statistically significant skew remained

III.2.1.2.2) CMDI subscale means by Discomfort PD High

Means of CMDI subscales by Discomfort PD group are given in Table III.2.1.2.2. The Mood, Evaluative, Vegetative and Total CMDI scores are significantly higher in the high Discomfort PD group compared to the low Discomfort PD group.

TABLE III.2.1.2.2) T-TEST RESULTS FOR DIFFERENCES IN MEANS OF CMDI SUBSCALE SCORES BETWEEN HIGH AND LOW DISCOMFORT GROUPS (PD)

N=102	Discomfort (PD) group	N	Mean	SD	t	Sig. (2-tailed)
Mood±	High	50	**1.471.34**	**.19**	**3.65***	**<.001**
	Low	52		**.17**		
Evaluative±	High	50	**1.41**	**.18**	**4.13*,#**	**<.001**
	Low	52	**1.27**	**.16**		
Vegetative	High	50	**40.68**	**10.69**	**2.66***	**.009**
	Low	52	**35.46**	**9.07**		
Total±	High	50	**1.98**	**.13**	**3.99***	**<.001**
	Low	52	**1.88**	**.13**		

*p<0.01

±Log transformation

#After transformation statistically significant skew remained

III.2.2) Illness Intrusiveness

Hypothesis 3.2

Those who report higher levels of pain will differ in the impact of illness intrusiveness from those who report higher levels of discomfort. Precisely, means testing will be performed on pain and discomfort PD groups to determine how illness intrusiveness is linked to reported pain and reported discomfort. SD, SOPA, MSIS and FIS will be tested.

Test of the differences in means (t-test) were completed on the Pain/Discomfort PD scale: high pain versus low pain; high discomfort versus low discomfort to determine links to illness intrusiveness. The high Pain PD and Discomfort PD group were linked to high emotional and disease SD scores. When examined by individual domains of the SD, those with high scores on the Pain PD and Discomfort PD had higher means for the question 'in pain versus comfortable' compared with their low counterparts but only high Discomfort PD had higher means on the 'Ill versus healthy' question when compared with their low counterparts. Both high Pain PD and high Discomfort PD had higher means for the SOPA subscale Disability, when compared with their low counterparts. However, only high Discomfort PD had higher means for the subscale Solicitude when compared with their low counterparts. Both high Pain PD and high

Discomfort PD had higher means for Emotional and Total MSIS when compared with their low counterparts. Whereas only high Pain PD had a higher mean for the Physical MSIS when compared with their low counterparts. The hypothesis was supported: Those who report higher levels of pain will differ in the impact of illness intrusiveness from those who report higher levels of discomfort. However, illness intrusiveness was impacted with both high pain and high discomfort, not in terms of overall impact but in domains of impact.

III.2.2.1) SD by PD

Tests on the parametric assumptions of the variable were completed to test for normality of the data and equality of the variance. Tests of skew (skewness/standard error of the skew was <2.58) showed that there was not significant skew at the $p<0.01$ level. Tests of kurtosis (kurtosis/standard error of the kurtosis was <2.58) showed that there was not significant kurtosis at the $p<0.01$ level. The results of Levene's test were not significant, indicating that the assumption of equal variances was reasonable.

III.2.2.1.1) Total Emotional (SD) - by PD

Means of Emotional SD score by Pain PD group are compared in Table III.2.2.1.1.A. The Emotional SD score is significantly higher in the high Pain PD group compared to the low Pain PD group. Means of Emotional SD score by Discomfort PD group are compared in Table III.2.2.1.1.B. The Emotional SD score is significantly higher in the high Discomfort PD group compared to the low Discomfort PD group.

TABLE III.2.2.1.1.A) T-TEST RESULTS FOR DIFFERENCES IN MEANS OF THE EMOTIONAL SUBSCALE SCORE FOR THE SD BETWEEN HIGH AND LOW PAIN GROUPS (PD)

N=102	Pain (PD) group	N	Mean	SD	t	Sig. (2-tailed)
Total emotional (SD)	High	48	**22.67**	**8.31**	**3.51***	**.001**
	Low	54	**16.85**	**8.39**		

*$p<0.01$

TABLE III.2.2.1.1.B) T-TEST RESULTS FOR DIFFERENCES IN MEANS OF THE EMOTIONAL SUBSCALE SCORE FOR THE SD BETWEEN HIGH AND LOW DISCOMFORT GROUPS (PD)

N=102	Discomfort (PD) group	N	Mean	SD	t	Sig. (2-tailed)
Total emotional (SD)	High	50	**23.00**	**8.21**	**4.13***	**<.001**
	Low	52	**16.31**	**8.15**		

*p<0.01

III.2.2.1.2) Total Disease (SD) - by PD

Means of Disease SD score by Pain PD group are compared in Table III.2.2.1.2.A. The Disease SD score is significantly higher in the high Pain PD group compared to the low Pain PD group. Means of Disease SD score by Discomfort PD group are compared in Table III.2.2.1.2.B. The Disease SD score is significantly higher in the high Discomfort PD group compared to the low Discomfort PD group.

TABLE III.2.2.1.2.A) T-TEST RESULTS FOR DIFFERENCES IN MEANS OF THE DISEASE SUBSCALE SCORE FOR THE SD BETWEEN HIGH AND LOW PAIN GROUPS (PD)

N=102	Pain (PD) group	N	Mean	SD	t	Sig. (2-tailed)
Total Disease (SD)	High	48	**12.08**	**3.78**	**3.42***	**.001**
	Low	54	**9.80**	**2.97**		

*p<0.01

TABLE III.2.2.1.2.B) T-TEST RESULTS FOR DIFFERENCES IN MEANS OF THE SD'S DISEASE SUBSCALE SCORE BETWEEN HIGH AND LOW DISCOMFORT GROUPS (PD)

N=102	Discomfort (PD) group	N	Mean	SD	t	Sig. (2-tailed)
Total Disease (SD)	High	50	**11.90**	**3.60**	**2.98***	**.004**
	Low	52	**9.88**	**3.23**		

*p<0.01

III.2.2.1.3) Disease Questions (SD) - by PD

Means of individual Disease SD questions by Pain PD group are compared in Table III.2.2.1.3.A. The 'Comfortable' versus 'In Pain' SD question score is significantly higher in the high pain PD group compared to the low Pain PD group. Means of Disease SD score by Discomfort PD group are compared in

Table III.2.2.1.3.B. The Disease SD question scores for 'Healthy' versus 'Ill' and 'Comfortable' versus 'In Pain' are significantly higher in the high Discomfort PD group compared to the low Discomfort PD group.

TABLE III.2.2.1.3.A) T-TEST RESULTS FOR DIFFERENCES IN MEAN LEVEL OF ENDORSEMENT OF SPECIFIC ITEMS ON THE SD'S DISEASE SUBSCALE SCALE BETWEEN HIGH AND LOW PAIN GROUPS (PD)

N=102	Pain (PD) group	N	Mean	SD	t	Sig. (2-tailed)
Ill	High	48	2.21	1.18	1.48	.141
	Low	54	1.85	1.25		
Disabled	High	48	2.81	1.10	0.33	.742
	Low	54	2.74	1.09		
In pain	High	48	**2.31**	**1.10**	**5.67***	**<.001**
	Low	54	**1.17**	**0.95**		
Fatigued	High	48	2.73	1.14	1.68	.096
	Low	54	2.37	1.02		

*p<0.01

TABLE III.2.2.1.3.B) T-TEST RESULTS FOR DIFFERENCES IN MEAN LEVEL OF ENDORSEMENT OF SPECIFIC ITEMS ON THE SD'S DISEASE SUBSCALE SCALE BETWEEN HIGH AND LOW DISCOMFORT GROUPS (PD)

N=102	Discomfort (PD) group	N	Mean	SD	t	Sig. (2-tailed)
Ill	High	50	**2.34**	**1.19**	**2.68***	**.009**
	Low	52	**1.71**	**1.18**		
Disabled	High	50	2.82	1.14	0.41	.681
	Low	52	2.73	1.05		
In pain	High	50	**2.18**	**1.08**	**4.38***	**<.001**
	Low	52	**1.25**	**1.06**		
Fatigued	High	50	2.68	1.13	1.29	.201
	Low	52	2.40	1.03		

*p<0.01

III.2.2.2) SOPA by PD

Tests on the parametric assumptions of the variable were completed to test for normality of the data and equality of the variance. Tests of skew (skewness/standard error of the skew was <2.58) showed that there was not significant skew at the p<0.01 level. Tests of kurtosis (kurtosis/standard error of the kurtosis was <2.58) showed that there was not significant kurtosis at the

$p<0.01$ level. The results of Levene's test were not significant, indicating that the assumption of equal variances was reasonable. Following these tests of assumptions, means of SOPA subscales by Pain PD group are given in Table III.2.2.2.A. The score for disability (SOPA) was significantly higher in the high Pain PD group compared with the low Pain PD group. Means of SOPA subscales by Discomfort PD group are given in Table III.2.2.2.B. The scores for disability and solicitude (SOPA) were significantly higher in the high Discomfort PD group compared with the low Discomfort PD group.

TABLE III.2.2.2.A) T-TEST RESULTS FOR DIFFERENCES IN MEANS OF THE SOPA SUBSCALE SCORES BETWEEN HIGH AND LOW PAIN GROUPS (PD)

N=84 (Only given to those reporting some pain)	Pain (PD) group	N	Mean	SD	t	Sig. (2-tailed)
Control	High	45	17.09	5.77	-0.86	.393
	Low	39	19.67	6.55		
Disability	High	45	**22.49**	**6.90**	**4.22***	**<.001**
	Low	39	**17.64**	**6.86**		
Harm	High	45	16.04	5.31	2.15	.034
	Low	39	14.69	5.917		
Emotion	High	45	14.18	5.54	1.56	.121
	Low	39	13.67	6.494		
Medication	High	45	16.13	4.68	2.19	.031
	Low	39	15.00	5.89		
Solicitude	High	45	9.84	5.94	2.36	.020
	Low	39	7.49	5.67		
Medical Cure	High	45	17.13	6.01	2.06	.042
	Low	39	16.21	5.48		

*$p<0.01$

TABLE III.2.2.2.B) T-TEST RESULTS FOR DIFFERENCES IN MEANS OF THE SOPA SUBSCALE SCORES BETWEEN HIGH AND LOW DISCOMFORT GROUPS (PD)

N=84 (Only given to those reporting some pain)	Discomfort (PD) group	N	Mean	SD	t	Sig. (2-tailed)
Control	High	46	17.50	5.85	-1.28	.206
	Low	38	19.24	6.64		
Disability	High	46	**23.00**	**6.73**	**4.21***	**<.001**
	Low	38	**16.89**	**6.50**		
Harm	High	46	15.89	5.29	8.52	.397
	Low	38	14.84	6.99		
Emotion	High	46	15.15	5.36	2.09	.040
	Low	38	12.47	6.41		
Medication	High	46	16.37	4.46	1.47	.146
	Low	38	14.68	6.05		
Solicitude	High	46	**10.35**	**5.70**	**2.85***	**.006**
	Low	38	**6.82**	**5.61**		
Medical Cure	High	46	17.59	5.94	1.56	.122
	Low	38	15.63	5.42		

*$p<0.01$

III.2.2.3) MSIS by PD

Tests on the parametric assumptions of the variable were completed to test for normality of the data and equality of the variance. Tests of skew (skewness/standard error of the skew was <2.58) showed that there was not significant skew at the $p<0.01$ level. Tests of kurtosis (kurtosis/standard error of the kurtosis was <2.58) showed that there was not significant kurtosis at the $p<0.01$ level. The results of Levene's test were not significant, indicating that the assumption of equal variances was reasonable.

III.2.2.3.1) MSIS subscale means by Pain PD group (high/low)

Means of MSIS subscales by Pain PD group are given in Table III.2.2.3.1. The Physical, Emotional and Total MSIS scores are significantly higher in the high Pain PD group compared to the low Pain PD group.

TABLE III.2.2.3.1) T-TEST RESULTS FOR DIFFERENCES IN MEANS OF THE MSIS SUBSCALE SCORES BETWEEN HIGH AND LOW PAIN GROUPS (PD)

N=102	Pain (PD)	N	Mean	SD	t	Sig. (2-tailed)
Physical	High	48	**70.92**	**16.77**	**3.14***	**.002**
	Low	54	**60.72**	**16.01**		
Emotional	High	48	**25.96**	**7.94**	**3.97***	**<.001**
	Low	54	**19.91**	**7.44**		
Total	High	48	**96.88**	**22.22**	**3.86***	**<.001**
	Low	54	**80.63**	**20.25**		

*p<0.01

III.2.2.3.2) MSIS subscale means by Discomfort PD group (high/low)

Means of MSIS subscales by Discomfort PD group are given in Table III.2.2.3.2. The Emotional and Total MSIS scores are significantly higher in the high Discomfort PD group compared to the low Discomfort PD group. The Physical subscale (MSIS) scores were not significantly different for the Discomfort PD groups.

TABLE III.2.2.3.2) T-TEST RESULTS FOR DIFFERENCES IN MEANS OF THE MSIS SUBSCALE SCORES BETWEEN HIGH AND LOW DISCOMFORT GROUPS (PD)

N=102	Discomfort (PD)	N	Mean	SD	t	Sig. (2-tailed)
Physical	High	50	68.72	16.90	1.88	.063
	Low	52	62.44	16.83		
Emotional	High	50	**26.28**	**7.75**	**4.66***	**<.001**
	Low	52	**19.37**	**7.23**		
Total	High	50	**95.00**	**22.27**	**3.07***	**.003**
	Low	52	**81.81**	**21.19**		

*p<0.01

III.3) COGNITIVE BIAS - HYPOTHESIS 4

Cognitive bias has been demonstrated in other pain populations and is generally linked to poor coping methods. The purpose of this study was to determine whether this bias would also be evident in the context of a chronic neurological disease, where patients may have many additional health concerns. Specifically, the purpose was to investigate the presence and characteristics of cognitive bias in MS patients.

III.3(1) STEM COMPLETION

Tests on the parametric assumptions of the variable were completed to test for normality of the data and equality of the variance. Certain tests of skew (skewness/standard error of the skew were $\geq$2.58) showed that there was significant skew at the $p<0.01$ level. Tests of kurtosis (kurtosis/standard error of the kurtosis was <2.58) showed that there was not significant kurtosis at the $p<0.01$ level. In cases where the data were skewed, transformation was completed, using Log transformation. This new variable without skew was used. The results of Levene's test were not significant, indicating that the assumption of equal variances was reasonable.

Hypothesis 4.1) Word Production and MS Bias

The hypothesis was that patients would exhibit a cognitive bias in word production towards MS-related stimuli. The bias would be mediated by anxiety and coping style. Those patients employing an emotional coping style would show the most cognitive bias.

Specifically, patients will demonstrate a cognitive bias on the stem completion task by choosing a significantly different number of completing responses that are MS related. The mean number of MS related responses would be significantly different by HADS anxiety scores. The mean number of MS related responses would be significantly different for those patients reporting emotional coping (SOPA and CMSS).

There was no relationship between HADS scores and the number of MS related responses. However, patients reporting more problem solving on the CMSS produced fewer illness and/or MS completions.

Hypothesis 4.2) Word Production and Pain Bias

The hypothesis was that patients would exhibit a cognitive bias in word production towards pain-related stimuli, mediated by anxiety and coping style. Those patients employing an emotional coping style will show the most cognitive bias.

Precisely, patients will demonstrate a cognitive bias on the stem completion task by choosing a significantly different number of completing responses that are pain- related. The number of pain-related responses will be

significantly different by HADS anxiety scores. The number of pain-related responses will be significantly different by McGill intensity score and 'Comfortable' vs. 'In Pain' SD question. The mean number of pain-related responses will be significantly different for those patients reporting emotional coping (SOPA and CMSS).

HADS, McGill intensity score scores, and 'Comfortable' vs. 'In Pain' (SD) question did not have any significant relationship with number of pain completions. However, there was a difference when the SOPA was examined. Those patients with Emotional awareness (SOPA) produced fewer sensory completions.

To summarize the sentence completion results, measures were investigated to determine their influence on the stem completion task. In means testing of the SOPA, those participants who were high on the Emotional awareness (SOPA) subscale were significantly less likely to make sensory completions. In means testing of the CMSS, those with a high Problem Solving (CMSS) subscale score were significantly less likely to use illness completions and the combination of illness and MS completions. Details by specific measure are given in Sections III.3(1).1-2.

III.3(1).1) Pain Self-Report by Stem Completion

Means testing for neither the In Pain versus Comfortable SD question nor the McGill Pain Intensity score showed any significant differences. However, the SOPA did show significant differences.

For means testing (t-test) of Stem Completion responses by SOPA subgroups (high/low) there were no significant differences found by Medical Cure, Control, Disabling, Harm, Solicitude, or Medication (SOPA). The only significant difference by group was for emotion, with those high on emotional awareness making fewer sensory completions, as shown in Table III.3(1).2.1.

III.3(1).2) Emotional Assessment by Stem Completion

There were no significant differences in means by HADS groups (high/low) or CMDI groups. However, the CMSS did show significant differences. There were no significant differences for CMSS Acceptance, Social Support, Energy Conservation or Physical Assistance. Comparisons for CMSS subgroup Problem

Solving did show differences. In summary, those low on problem solving made more illness, and illness and MS completions. These data are shown in Tables III.3(1).2.2.A-D.

TABLE III.3(1).2.1) T-TEST RESULTS FOR DIFFERENCES IN MEANS OF STEM COMPLETION SUBGROUP SCORES BETWEEN HIGH AND LOW EMOTION SUBSCALE GROUPS (SOPA)

N=84	Emotion (SOPA) group	N	Mean	SD	t	Sig. (2-tailed)
Sensory completion	High	44	**1.50**	**1.13**	**-2.81***	**.006**
	Low	40	**2.28**	**1.40**		
Affective completion	High	44	2.07	1.15	0.29	.772
	Low	40	2.00	0.99		
Illness completion	High	44	3.64	1.56	0.49	.629
	Low	40	3.48	1.49		
MS completion±	High	44	0.18	0.18	-0.47	.643
	Low	40	0.20	0.19		
Sensory and affective	High	44	3.57	1.77	-1.83	.071
	Low	40	4.28	1.77		
Illness and MS	High	44	4.27	1.82	0.18	.855
	Low	40	4.20	1.81		
All four	High	44	7.84	2.83	-1.09	.279
	Low	40	8.48	2.47		

*$p<0.01$

±Log transformation

TABLE III.3(1).2.2.A) T-TEST RESULTS FOR DIFFERENCES IN MEANS OF STEM COMPLETION SUBGROUP SCORES BETWEEN HIGH AND LOW EMOTIONAL RELEASE SUBSCALE GROUPS (CMSS)

N=102	Emotional release (CMSS) group	N	Mean	SD	t	Sig. (2-tailed)
Sensory completion	High	44	1.84	1.41	-0.15	.884
	Low	58	1.88	1.23		
Affective completion	High	44	2.09	1.05	0.51	.608
	Low	58	1.98	1.05		
Illness completion	High	44	3.14	1.55	-2.17	.032
	Low	58	3.79	1.48		
MS completion±	High	44	0.16	0.18	-1.36	.178
	Low	58	0.21	0.19		
Sensory and affective	High	44	3.93	1.91	0.20	.844
	Low	58	3.86	1.65		
Illness and MS	High	44	3.70	1.84	-2.52	.013
	Low	58	4.59	1.69		
All four	High	44	7.64	2.89	-1.55	.125
	Low	58	8.45	2.42		

±Log transformation

TABLE III.3(1).2.2.B) T-TEST RESULTS FOR DIFFERENCES IN MEANS OF STEM COMPLETION SUBGROUP SCORES BETWEEN HIGH AND LOW PROBLEM SOLVING SUBSCALE GROUPS (CMSS)

N=102	Problem solving (CMSS) group	N	Mean	SD	t	Sig. (2-tailed)
Sensory completion	High	50	1.84	1.18	-0.17	.864
	Low	52	1.88	1.42		
Affective completion	High	50	2.08	0.80	0.48	.635
	Low	52	1.98	1.24		
Illness completion	High	50	**2.88**	**1.34**	**-4.40***	**<.001**
	Low	52	**4.12**	**1.49**		
MS completion±	High	50	0.17	0.19	-1.07	.285
	Low	52	0.21	0.19		
Sensory and affective	High	50	3.92	1.51	0.16	.876
	Low	52	3.87	1.98		
Illness and MS	High	50	**3.50**	**1.57**	**-4.19***	**<.001**
	Low	52	**4.88**	**1.76**		
All four	High	50	7.42	2.20	-2.61	.010
	Low	52	8.75	2.89		

*$p<0.01$

±Log transformation

TABLE III.3(1).2.2.C) T-TEST RESULTS FOR DIFFERENCES IN MEANS OF STEM COMPLETION SUBGROUP SCORES BETWEEN HIGH AND LOW AVOIDANCE SUBSCALE GROUPS (CMSS)

N=102	Avoidance (CMSS) group	N	Mean	SD	t	Sig. (2-tailed)
Sensory completion	High	35	2.00	1.14	0.77	.445
	Low	67	1.79	1.39		
Affective completion	High	35	2.31	1.05	2.01	.047
	Low	67	1.88	1.02		
Illness completion	High	35	3.31	1.35	-0.93	.357
	Low	67	3.61	1.62		
MS completion[±]	High	35	0.19	0.20	0.005	.996
	Low	67	0.18	0.18		
Sensory and affective	High	35	4.31	1.64	1.77	.079
	Low	67	3.67	1.79		
Illness and MS	High	35	4.03	1.77	-0.72	.474
	Low	67	4.30	1.82		
All four	High	35	8.34	2.59	0.67	.502
	Low	67	7.97	2.69		

[±]Log transformation

TABLE III.3(1).2.2.D) T-TEST RESULTS FOR DIFFERENCES IN MEANS OF STEM COMPLETION SUBGROUP SCORES BETWEEN HIGH AND LOW PERSONAL HEALTH CONTROL SUBSCALE GROUPS (CMSS)

N=102	Personal health control (CMSS) group	N	Mean	SD	t	Sig. (2-tailed)
Sensory completion	High Low	45 57	1.87 1.86	1.27 1.34	0.03	.979
Affective completion	High Low	45 57	2.00 2.05	1.02 1.08	-0.25	.803
Illness completion	High Low	45 57	3.13 3.81	1.38 1.61	-2.24	.028
MS completion±	High Low	45 57	0.20 0.18	0.18 0.19	0.37	.710
Sensory and affective	High Low	45 57	3.87 3.91	1.80 1.74	-0.13	.897
Illness and MS	High Low	45 57	3.84 4.49	1.76 1.79	-1.82	.071
All four	High Low	45 57	7.71 8.40	2.73 2.56	-1.32	.191

±Log transformation

III.3(2) EXPERIMENTAL RECALL

Tests on the parametric assumptions of the variable were completed to test for normality of the data and equality of the variance. Certain tests of skew (skewness/standard error of the skew were ≥ 2.58) showed that there was significant skew at the $p<0.01$ level. Tests of kurtosis (kurtosis/standard error of the kurtosis was <2.58) showed that there was not significant kurtosis at the $p<0.01$ level. In cases where the data were skewed, transformation was completed, using Log transformation. This new variable without skew and kurtosis was used. If any of the results of Levene's test were significant, the t-test value corresponding to 'equal variance not assumed' was used and a footnote to indicate this was included.

Hypothesis 4.3) Recall and MS Bias

The hypothesis was that patients would exhibit a cognitive bias in recall towards MS -related stimuli. The bias will be mediated by anxiety and linked to coping style. Those patients employing an emotional coping style will show the most cognitive bias.

Precisely, patients will demonstrate a cognitive bias on the experimental recall task by recalling more words that are MS -related. The number of MS -related responses will be significantly different by HADS anxiety scores. The number of MS -related responses will be significantly different by subgroups on the CMSS. Those patients reporting emotional coping (SOPA and CMSS) will recall the most MS -related words.

There was no relationship between HADS Anxiety, HADS Depression, CMDI Depression score or the CMSS and MS-related recall. This does not support hypothesis 4.3. Details by specific measure will be outlined in Sections 3(2).2.1-3.

Hypothesis 4.4) Recall and Pain Bias

The hypothesis was that patients would exhibit a cognitive bias in recall towards sensory and affective pain-related stimuli. The bias will be mediated by anxiety and linked to coping style. Those patients employing an emotional coping style will show the most cognitive bias.

Precisely, patients will demonstrate a cognitive bias on the experimental recall task by recalling significantly different numbers of words that are sensory and affective pain-related. The numbers of sensory and affective pain-related responses will be significantly different by McGill intensity score and 'Comfortable' vs. 'In Pain' (SD) question. The numbers of sensory and affective pain-related responses will be significantly different by HADS anxiety scores. The numbers of sensory and affective pain-related responses will be significantly different based on scores on the CMSS. Those patients reporting emotional coping (SOPA and CMSS) will recall the most sensory and affective pain-related words.

The results show that the number of sensory and affective pain-related responses was not significantly different by McGill intensity score. The number of

sensory and affective pain-related-related responses was not significantly different by anxiety and depression scores. However, those low on Acceptance (CMSS) recalled more affective words. This implies that coping mediates cognitive bias. Details by specific measure will be outlined in Sections 3(2).2.1-3.

III.3(2).1) Pain Self-Report by Experimental Recall

A test of the difference in means (t-test) was performed on the ERLT for emotional SD, disease SD, disease questions (high/low) and McGill Total Intensity score high/low however, there were no significant differences found. SOPA subscales were also unrelated to any of the semantic categories on the ERLT.

III.3(2).2) Emotional Assessment by Experimental Recall

There was no significant relationship between the McGill intensity score or the 'Comfortable' vs. 'In Pain' (SD) question and number of pain words recalled. This does not support the hypothesis that pain words recall will differ by pain intensity. There were also no significant differences found between the HADS anxiety or depression or the CMDI score and recall. This does not support the hypothesis that mood state will affect recall of pain words.

III.3(2).2.1) HADS by Experimental Recall

Difference in means tests (t-test) of Experimental Recall task by HADS Anxiety and Depression groups (high/low) are given in Tables III.3(2).2.1.A-B.

TABLE III.3(2).2.1.A) T-TEST RESULTS FOR DIFFERENCES IN MEANS OF EXPERIMENTAL RECALL VERBAL LEARNING TASK SUBGROUP SCORES BETWEEN HIGH AND LOW ANXIETY SUBSCALE GROUPS (HADS)

N=102	Anxiety (HADS)	N	Mean	SD	t	Sig. (2-tailed)
Correct responses	High	43	26.70	10.73	-1.23	.223
	Low	59	29.34	10.77		
Neutral words	High	43	4.00	2.68	0.60	.550
	Low	59	3.69	2.43		
Sensory words	High	43	4.58	3.02	-1.99	.049
	Low	59	5.69	2.61		
Affective words[±]	High	43	0.61	0.32	-0.11	.914
	Low	59	0.62	0.30		
MS words[±]	High	43	0.61	0.29	-1.37	0.175
	Low	59	0.68	0.25		

[±]Log transformation

TABLE III.3(2).2.1.B) T-TEST RESULTS FOR DIFFERENCES IN MEANS OF EXPERIMENTAL RECALL VERBAL LEARNING TASK SUBGROUP SCORES BETWEEN HIGH AND LOW DEPRESSION SUBSCALE GROUPS (HADS)

N=102	Depression (HADS)	N	Mean	SD	t	Sig. (2-tailed)
Correct responses	High	34	26.82	9.88	-0.93	.355
	Low	68	28.93	11.20		
Neutral words	High	34	3.74	2.66	-0.25	.805
	Low	68	3.87	2.49		
Sensory words	High	34	4.29	2.29	-2.41	.018
	Low	68	5.69	2.97		
Affective words±	High	34	0.58	0.33	-0.77	.443
	Low	68	0.63	0.29		
MS words±	High	34	3.88	2.80	-95	.347
	Low	68	4.41	2.91		

±Log transformation

III.3(2).2.2) CMDI by Experimental Recall

Differences in means between CMDI high/low on the Experimental Recall semantic categories are shown in Table III.3(2).2.2.A. When the CMDI is split into its subcomponents, none of the subscales showed any relationship to the ERLT as shown in Table II.3(2)2.2.B. These differences do not reflect overall memory, as number of correct answers was not statistically different.

TABLE III.3(2).2.2.A) T-TEST RESULTS FOR DIFFERENCES IN MEANS OF EXPERIMENTAL RECALL VERBAL LEARNING TASK SUBGROUP SCORES BETWEEN HIGH AND LOW DEPRESSION GROUPS (CMDI)

N=102	CMDI (total)	N	Mean	SD	t	Sig. (2-tailed)
Correct	High	42	27.29	9.92	.735	.464
	Low	60	28.88	11.38		
Neutral words	High	42	4.02	2.67	-0.667	.506
	Low	60	3.68	2.44		
Sensory words	High	42	4.55	2.44	2.06	.042
	Low	60	5.70	3.00		
Affective words±	High	42	0.59	0.32	-0.77	.444
	Low	60	0.64	0.30		
MS words±	High	42	0.65	0.28	-0.03	.978
	Low	60	0.65	0.26		

±Log transformation

TABLE III.3(2).2.2.B) T-TEST RESULTS FOR DIFFERENCES IN MEANS OF EXPERIMENTAL RECALL VERBAL LEARNING TASK SUBGROUP SCORES BETWEEN HIGH AND LOW VEGETATIVE SUBSCALE GROUPS (CMDI)

N=102	CMDI (vegetative)	N	Mean	SD	t	Sig. (2-tailed)
Correct	High	51	26.69	11.39	-1.45	.150
	Low	51	26.76	9.99		
Neutral words	High	51	3.76	2.91	-0.23	.816
	Low	51	3.88	2.11		
Sensory words	High	51	4.51	2.30	-2.63^	.010
	Low	51	5.94	3.13		
Affective words±	High	51	0.57	0.29	-1.49	.141
	Low	51	0.66	0.24		
MS words±	High	51	0.63	0.29	-0.71	.480
	Low	51	0.67	0.24		

±Log transformation

^equal variances not assumed

III.3(2).2.3) CMSS by Experimental Recall

CMSS Social Support, Energy Conservation, Problem Solving, Physical Assistance and Personal Health Control did not show any significant differences on t-tests for CMSS high versus low on the semantic categories of the ERLT. However, difference in means tests (t-test) of ERLT categories by CMSS subgroup Acceptance did show significant differences and are given in Tables III.3(2).2.3.A-C. Those low on acceptance recalled more affective words.

TABLE III.3(2).2.3.A) T-TEST RESULTS FOR DIFFERENCES IN MEANS OF EXPERIMENTAL RECALL VERBAL LEARNING TASK SUBGROUP SCORES BETWEEN HIGH AND LOW ACCEPTANCE SUBSCALE GROUPS (CMSS)

N=102	Acceptance (CMSS)	N	Mean	SD	t	Sig. (2-tailed)
Correct responses	High	49	26.22	9.52	-1.82	.071
	Low	53	30.08	11.61		
Neutral words	High	49	3.71	2.28	-0.42	.677
	Low	53	3.92	2.76		
Sensory words	High	49	5.41	2.75	0.63	.533
	Low	53	5.06	2.92		
Affective words±	High	49	**0.53**	**0.26**	**-2.72***	**.008**
	Low	53	**0.69**	**0.26**		
MS words±	High	49	3.69	2.38	-1.57	.120
	Low	53	4.74	3.21		

*p<0.01

±Log transformation

TABLE III.3(2).2.3.B) T-TEST RESULTS FOR DIFFERENCES IN MEANS OF EXPERIMENTAL RECALL VERBAL LEARNING TASK SUBGROUP SCORES BETWEEN HIGH AND LOW EMOTIONAL RELEASE SUBSCALE GROUPS (CMSS)

N=102	Emotional release (CMSS) group	N	Mean	SD	T	Sig. (2-tailed)
Correct responses	High	44	27.52	10.05	-0.57	.569
	Low	58	28.76	11.36		
Neutral words	High	44	3.68	2.68	-0.49	.625
	Low	58	3.93	2.43		
Sensory words	High	44	5.64	2.62	1.28	.203
	Low	58	4.91	2.96		
Affective words[±]	High	44	0.60	0.29	-0.41	.679
	Low	58	0.63	0.32		
MS words[±]	High	44	0.59	0.28	-2.03	.045
	Low	58	0.69	0.2		

[±]Log transformation

TABLE III.3(2).2.3.C) T-TEST RESULTS FOR DIFFERENCES IN MEANS OF EXPERIMENTAL RECALL VERBAL LEARNING TASK SUBGROUP SCORES BETWEEN HIGH AND LOW AVOIDANCE SUBSCALE GROUPS (CMSS)

N=102	Avoidance (CMSS) group	N	Mean	SD	t	Sig. (2-tailed)
Correct responses	High	35	27.29	9.95	-0.64	.527
	Low	67	28.72	11.23		
Neutral words	High	35	3.11	2.01	-2.28	.025
	Low	67	4.19	2.70		
Sensory words	High	35	5.06	2.68	-0.43	.666
	Low	67	5.31	2.92		
Affective words±	High	35	0.58	0.30	-0.63	.529
	Low	67	0.63	0.31		
MS words±	High	35	0.67	0.22	0.54	.590
	Low	67	0.64	0.29		

±Log transformation

III.3(3) HAYLING SENTENCE COMPLETION

Tests on the parametric assumptions of the variable were completed to test for normality of the data and equality of the variance. Certain tests of skew (skewness/standard error of the skew were ≥ 2.58) showed that there was significant skew at the $p<0.01$ level. Certain other tests of kurtosis (kurtosis/standard error of the kurtosis were ≥ 2.58) showed that there was significant kurtosis at the $p<0.01$ level. In cases where the data were skewed and/or showed significant kurtosis, transformation was completed, first using Log transformation and if necessary, square root transformation. The first transformation showing a new variable without skew and kurtosis was used. If neither transformation significantly reduced the skew and/or kurtosis to bring it/them within acceptable levels, the transformation showing the most reduction in skew was used (as the skew is generally considered more of a problem than kurtosis when it deviates from normality) and a footnote to indicate this is included. Such results should be interpreted with caution. If any of the results of

Levene's test were significant, the t-test value corresponding to 'equal variance not assumed' was used and a footnote to indicate this was included.

Hypothesis 4.5) Latency to Respond and Pain Bias

The hypothesis was that patients would exhibit a cognitive bias towards pain-related stimuli.

Precisely, patients with pain will exhibit slower response rates to the incongruent Hayling Brixton test than those without pain. Response time to complete pain-related sentences (both congruent and incongruent sentences) will be significantly linked to McGill intensity score and 'Comfortable' vs. 'In Pain' (SD) question with those with high scores taking longer to complete pain-related sentences. Response time to complete pain-related sentences will be significantly longer for incongruent sentences than congruent sentences for patients with high McGill intensity scores and 'Comfortable' vs. 'In Pain' (SD) question. Error rates will be significantly linked to McGill intensity score and 'Comfortable' vs. 'In Pain' (SD) question with high scorers making more errors on the incongruous pain sentences than low scorers on the incongruous pain sentences.

It was hypothesized that patients would exhibit a cognitive bias towards pain-related stimuli. However, there were no significant relationships between the McGill intensity score or the 'Comfortable' vs. 'In Pain' (SD) question and Hayling times or error rates. This does not support Hypothesis 4.5.

Patients with pain did not exhibit slower response rates to the incongruent Hayling Brixton test than those without pain. Response time to complete pain-related sentences was not significantly different for incongruent sentences or congruent sentences for patients with high McGill intensity scores or for those with high SD scores. Error rates were not significantly linked to McGill intensity score and were not significantly different by pain attitude (SOPA).

There were no differences with regard to the speed component of The Hayling Sentence Completion Task. There were also no differences when examining the error rate. There was no evidence of cognitive bias using the Hayling data. Details by measure will be outlined in Sections 3(3).1.

III.3(3).1) Pain Self-Report by Hayling Sentence Completion

There was no significant relationship for SD or for McGill Intensity score with the Hayling Sentence Completion. Error rates were examined for SD and McGill Intensity scores but no significant differences were found. SOPA was also examined for differences in means. Medical cure, Control, Disabling, Harm and Solicitude, Emotion and Medication (SOPA) did not show any significant differences. The data are shown in Tables III.3(3).1.A-B.

TABLE III.3(3).1.A) T-TEST RESULTS FOR DIFFERENCES IN MEANS OF HAYLING SENTENCE COMPLETION TASK SUBGROUP SCORES BETWEEN HIGH AND LOW EMOTION SUBSCALE GROUPS (SOPA)

N=84 (Only given to those reporting some pain)	Emotion (SOPA) group	N	Mean	SD	t	Sig. (2-tailed)
Pain error±	High	44	0.63	0.310.2	1.51	.136
	Low	40	0.54	5		
Non-pain error±	High	44	0.60	0.36	1.45	.151
	Low	40	0.50	0.30		
Mild errors pain	High	44	2.34	1.79	0.88^	.383
	Low	40	2.05	1.22		
Major errors pain±	High	44	0.19	0.27	1.28^,#	.205
	Low	40	0.12	0.18		
Mild errors non-pain	High	44	2.41	1.90	1.10	.273
	Low	40	1.98	1.69		
Major errors non-pain±	High	44	0.21	0.26	1.89#	.066
	Low	40	0.12	0.18		

±Log transformation

^Equal variances not assumed

#After transformation statistically significant skew remained

TABLE III.3(3).1.B) T-TEST RESULTS FOR DIFFERENCES IN MEANS OF HAYLING SENTENCE COMPLETION TASK SUBGROUP SCORES BETWEEN HIGH AND LOW MEDICATION SUBSCALE GROUPS (SOPA)

N=84 (Only given to those reporting some pain)	Medication (SOPA) group	N	Mean	SD	t	Sig. (2-tailed)
Pain error[±]	High	38	0.62	0.33	0.76	.047
	Low	46	0.57	0.24		
Non-pain error[±]	High	44	0.59	0.36	0.86	.391
	Low	40	0.52	0.33		
Mild errors pain	High	44	2.03	1.52	-0.95	.345
	Low	40	2.35	1.57		
Major errors pain[±]	High	44	0.23	0.27	2.52[^#]	.014
	Low	40	0.10	0.19		
Mild errors non-pain	High	44	2.29	2.00	0.40	.690
	Low	40	2.13	1.64		
Major errors non-pain[±]	High	44	0.20	0.26	1.09	.280
	Low	40	0.14	0.21		

[±]Log transformation

[^]Equal variances not assumed

[#]After transformation statistically significant skew remained

III.4) Summary of significant results

Hypothesis 1) Pain report

The only significant difference for McGill high/low pain group was for the SD question 'Comfortable' versus 'In Pain'. This does not support the hypothesis that not all of those with pain symptoms would report pain, however, most of the time those experiencing pain symptoms did report more pain on the semantic differential. The mean total McGill intensity score for those with medium to high pain was significantly higher than for those with low to no pain. This supports the hypothesis that patients reporting 'pain' when questioned will have a higher McGill pain intensity score than those not reporting 'pain'.

There were differences between the words chosen by the high McGill versus low McGill intensity groups; however the overall finding was that there was a larger overlap in the words chosen than there were differences between them. Therefore, the hypothesis was not supported, patients reporting 'pain' when questioned did not select a different pattern of adjectives from the McGill to describe qualitative aspects of their pain, than those not reporting 'pain'.

Hypothesis 2) Mood and Pain

There was a significant difference in HADS anxiety mean score for those with a high versus a low McGill intensity score. There were significant differences in HADS anxiety item means for high versus low McGill intensity score for items: frightened and restless. Those with more pain had higher anxiety but not depression.

There were significant differences in pain attitudes for those with high versus low pain, with those with high pain expecting a medical cure for their pain.

Hypothesis 3) Pain versus discomfort

Both Pain PD and Discomfort PD had higher means for Emotional and Total MSIS when compared with their low counterparts. Only the high Pain PD group had a higher mean for the Physical MSIS when compared with their low

counterparts. It appears that those who report higher levels of pain will differ in the impact of illness intrusiveness from those who report higher levels of discomfort. However, illness intrusiveness was impacted with both high pain and high discomfort, not in terms of overall impact but in domains of impact.

The score for disability (SOPA) was significantly higher in the high Pain PD group compared with the low Pain PD group, whereas the scores for both disability and solicitude (SOPA) were significantly higher in the high Discomfort PD group compared with the low Discomfort PD group.

Hypothesis 4) Cognitive bias

To summarize the sentence completion results, those participants who were high on the Emotional Awareness (SOPA) subscale were significantly less likely to make sensory completions. In means testing of the CMSS, those with a high Problem Solving (CMSS) subscale score were significantly less likely to use illness completions and the combination of illness and MS completions.

To summarize the experimental recall results although there were no differences in recall with regard to MS bias, there was a difference found for recall with regard to pain bias. Participants low on the Acceptance (CMSS) subscale recalled more affective pain words.

IV) DISCUSSION

Pain is still an under-recognised and apparently under-reported symptom in MS. The current study was conducted to characterise pain in MS and determine the psychological issues involved. Much was discovered about the types of words MS patients use to describe their sensory symptoms. There were issues highlighted such as the importance of anxiety and its relationship with pain. It was discovered that there were differences in illness intrusiveness for people who say they have discomfort versus those who say they have pain. There were alterations in cognitive bias based on coping styles. The sample had remarkably similar means to many other samples, implying that the phenomena noted are generalizable to MS more globally.

However, due to the fact that there were multiple comparisons made, caution must be exercised when generalizing to other samples and it will be important that there is replication of the results found in this study, although attempts were made to address this issue with these data. As a reminder, as there were multiple comparisons made, the alpha value, although appropriate for one test may not be appropriate for the set of comparisons. In order to reduce the risk of making a Type I error or the rejection of the null hypothesis when it is actually true, the alpha value was lowered. The most conservative approach is the Bonferroni correction which takes the alpha value and divides by the number of comparisons. However, the Bonferroni approach was not selected. Instead, the option of lowering the p value to $p<0.01$ (vs. $p<0.05$) was selected. The reason is that Bonferroni would have dramatically lowered the risk of Type I error, but at a cost of a corresponding increase in the risk of Type II error. Additionally, as this research was exploratory and involved integrating data from several areas in a new way, substantially increasing the possibility of failing to reject the null hypothesis when it was false was not an acceptable one. Any possible relationships, if significant, are best documented here. This will allow investigators to explore these relationships more fully and stringently test these findings in future studies.

There are clear clinical implications of these data although there are major limitations to the research in terms of sampling and methodology. In addition,

this study paves a path for additional research projects that may build upon these findings.

IV.1) MCGILL

To determine whether patients with more pain symptoms were different on other variables than those who did not say they had pain, the McGill Pain Intensity score was used. The patient population was split into two groups, high pain and low pain and these groups were compared on other measures.

High McGill was significantly associated with high mean on the 'In Pain' question of the SD. This was as expected as both address subjective pain and this is simply a validation of two types of questioning about subjective pain and also of reliability and consistency of patient self-report.

There was a significant difference in the mean number of McGill adjectives for those with medium to high "pain" versus those with low to no "pain". This was as expected as the McGill total score is partially based on number of adjectives. This illustrates that pain is not an all or none phenomena but represents a range of experience, as even those with a low McGill Intensity score, did have some adjectives to report.

There were differences in the words chosen by the high McGill Intensity group and low intensity McGill group. However, the majority of words occurred in both groups. The interesting issue is that patients reporting "pain" did not select a different pattern of adjectives from the McGill to describe qualitative aspects of their pain, than those not reporting "pain". It may be that many adjectives were the same in both groups because symptoms being described were similar. It may be more useful to focus on the different adjectives in order get at real differences between the high and low pain groups.

IV.1.1) Emotional Assessment

IV.1.1.1) Relationship of pain to anxiety and depression

Surprisingly, there were no significant differences for the mean of the HADS depression score, means for items being endorsed on the HADS depression scale, CMDI overall and by CMDI subgroup for those high versus low on the McGill Pain Impact Scale. Based on previous study, depression would have been thought to be important in pain experience. These lack of differences

may indicate that the relationship between depression and pain, as assessed by HADS, and McGill intensity score, may be isolated to a particular type of depression rather than to depression overall or that depression does not have as big a role in pain experience in this population. There has been a lot of speculation that depression in MS may sometimes have a biological etiology (Siegert and Abernethy, 2005). This would explain why there might not be a discernable relationship between pain and depression for the group as a whole. It may be that some depression is purely biologically based and pain may not play a role for this group of patients, thereby introducing noise into the data.

For anxiety, significant differences in mean for HADS anxiety score by McGill high/low were found. These results may indicate the true pervasive relationship between pain and anxiety. Previous research showing the cyclical nature of the anxiety and pain relationship (Hadjistavropoulos et al., 2004) supports this finding. Also, the specific items that were important in this relationship may indicate that the association between anxiety (as assessed by HADS) and McGill intensity score may be more specifically linked to fear (feeling frightened) and nervousness (feeling restless).

Previous research has shown that pain and mood disorders tend to occur together (Clark et al., 2000) although it is difficult to determine causality and the relationship may be bi directional or even cyclical. Archibald et al. (Archibald et al., 1994) found that those with pain had a lower mean score for the Mental Health Inventory (MHI) than for those without pain. A lower MHI score may in part be comparable to a higher HADS anxiety score.

The data show that in this sample, patients with more pain had higher anxiety and but not higher depression. The importance of anxiety in MS has not been fully recognized although it has been reported (Feinstein et al., 1999). The current study illustrates the impact that anxiety can have on other areas for patients.

IV.1.1.2) Illness Intrusiveness

The group with high McGill intensity scores tend to expect a medical cure for their pain. Previous research has found that belief in a medical cure is positively related to professional services utilization (Jensen and Karoly, 1992).

These high McGill intensity score individuals may have poorer overall outcome due to using poor coping strategies.

The group reporting high pain may do so with the expectation of a medical cure for their pain. It is possible that this group reports more pain in order to get others to do something about it. This same group has more emotional impact of MS (HADS anxiety). It may be that those who expect others to do something for their pain are more likely to be disappointed by others or by treatment and that this leads to more emotional disruption.

In summary for the relationship between the description of pain and pain intensity, it was discovered that although only 12% named pain as their major problem, 97% of participants selected at least one adjective from the McGill adjective list to describe their experience. The majority of patients stated they did not 'really have pain' but only 18% described themselves as completely pain free on a semantic differential measure. 70% chose more than six adjectives from the McGill to describe their sensations. The overall finding was that the most common descriptive adjectives are similar across pain intensity levels. This simply draws attention to the issue that pain is more likely to be a continuous variable rather than a dichotomous one.

Within a clinic population of MS patients, many responded to general questions about pain occurrence negatively, yet reported sensations that would count as "pain" in other populations. Perhaps, the distinction between "pain" and other aspects of the disease was more blurred for patients than professionals. There was a clear concurrence of adjectives selected to describe their physical sensations at both high and low levels of pain intensity, suggesting that a characteristic subjective profile of MS pain experience has emerged, based on this study, and will continue to do so in future studies. Clinically, this research highlights the importance of asking patients more generally about sensations and not relying on presence or absence of reported pain.

IV.1.1.3) Relationship between mood and pain intensity

MS carries an increased risk of psychiatric morbidity with or without pain, so it was expected that emotional distress links to pain in MS would be complex. It was discovered that HADS anxiety is a reasonable indicator of total McGill score. As for other factors that co-vary with anxiety, the most significant factor seems to

be type of MS, with SP having a greater incidence of HADS anxiety whereas disability (EDMUS score) gender or age do not seem to be associated with anxiety in this sample.

It is important to note that anxiety, and not depression, was significantly linked to pain intensity in MS, although depression is more commonly recognised to occur in MS in general. Factors such as age, gender and disability were not related to reported pain intensity. It is proposed that for patients with pain, formally assessing and addressing their anxiety may alleviate distress related to their pain.

Anxiety is not often addressed in MS patients by their clinicians and very few were receiving any treatment to attempt to modify their anxiety symptoms. Many were treated with anti-depressants by comparison. It seems that there is a need to try to use available anti-anxiety medications as well as non-medicinal options to treating anxiety in MS patients with the hope of alleviating their anxiety and possibly lessening the impact of related problems.

IV.2) PAIN/DISCOMFORT SCALE

To determine whether those who state they have pain were different from those who state they have discomfort, the Pain PD and Discomfort PD scales were used.

IV.2.1) Comparison of Pain and Discomfort Scales (PD)

The means for each question on the Pain PD were not significantly different from the means for the corresponding question on the Discomfort PD scale with the exception of "My pain/discomfort stops me from enjoying life". The Discomfort PD had a significantly different (higher) mean for this question. This was completed because this was one of the central questions, why do some patients who state they have no pain, choose so many items on the McGill Intensity Scale? Is pain and discomfort addressing the same issue, different issues or overlapping issues? The fact that many people were high on both scales and that those high on the Pain PD and Discomfort PD use many of the same descriptors would imply that these issues do measure some of the same information, as was initially suspected. However, the fact that the data were not exactly the same tells us that there is some difference in the information being gathered simply by changing the term.

IV.2.2) Emotion by PD

IV.2.2.1) HADS

Those with both pain and discomfort report high anxiety, implying that both issues are linked to higher distress. This may mean that even if pain and discomfort are measuring different types of pain, both types are important in terms of distress.

Depression (HADS) means were compared using Pain PD high vs. low groups and a significant difference was detected with high Pain PD and high Discomfort having a higher HADS depression. This was expected as depression has been linked to pain in previous studies (Magni et al., 1994; Holzberg et al., 1996; Clark et al., 2000). Therefore, in the current study, both pain and discomfort are linked to both areas of distress (anxiety and depression) and so it is important to be aware of and attempt to modify both of these mood disorders.

Specifically what the difference is between pain and discomfort has not yet been determined however, both appear important for distress. They may be on the same continuum or they may be truly different entities yet still cause some of the same psychological distress. The hope is that this study will begin to illustrate the importance of both 'pain' and 'discomfort' as concepts.

IV.2.2.2) CMDI

All CMDI subscale and total means were compared using Pain PD and Discomfort PD high vs. low groups. Significant differences were detected in all areas. Again, this lends support to the idea that both pain and discomfort are important regardless of their relationship with each other. It may be that pain and discomfort can be profound enough to cause problems in all areas addressed by the CMDI.

Further division of the sample or follow-up studies may be able to further describe the differences between pain and discomfort. However, with the data, as it is today, it is clear that both have a relationship distress and therefore, both should be inquired about and steps to intervene should be taken.

IV.2.3) Illness Intrusiveness

IV.2.3.1) SD

Both the high pain and high discomfort groups had higher means for emotional and disease impact of the SD compared to low pain and low discomfort groups respectively.

The most interesting finding is that the participants in the high discomfort group assessed their illness as worse than those participants in the low discomfort group but no difference was found on this item for high pain versus low pain. This may indicate that experiencing symptoms termed 'Pain' and those labelled 'Discomfort' are associated with a different degree of impact. One might have expected pain to have a stronger impact of the perception of healthy versus ill, but it appears that having more discomfort has a bigger impact in perception of illness. It may mean that the term 'pain' refers to physical pain and discomfort refers more to emotional pain or symptoms that typically would not be considered pain and may be more troubling. This may be indicating more illness intrusiveness in the high discomfort group but not the high pain group. Perhaps discomfort is a surrogate for level of illness intrusiveness. With this line of thinking, high pain as appropriate associations and high illness intrusiveness (discomfort) has appropriate associations.

IV.2.3.2) SOPA

The only difference that appears between high pain and discomfort PD measures is that only high discomfort PD is associated with high solicitude SOPA. Solicitude SOPA is the desire for others to be solicitous about one's pain. One might expect the high solicitous SOPA group to experience more pain and discomfort but it may be that those that are seeking emotional support are more likely to be experiencing emotional difficulty and are not able to find a good coping mechanism to modify its impact. This would also fit with the explanation that high discomfort equals high illness intrusiveness.

IV.2.3.3) MSIS

MSIS subscales and total means were compared using Pain and Discomfort PD high vs. low groups. For the high and low Pain PD groups, significant differences were detected in the physical and emotional subscales and in the total. For the high and low Discomfort PD groups, significant differences

were only detected in the emotional subscale and total but not in physical MSIS. This difference may indicate that experiencing symptoms termed 'Pain' rather than 'Discomfort' is associated with a higher degree of physical impact. Or, as was referred to in the previous section, that discomfort is used to describe pain that is not purely of a physical nature.

In summary, those who report higher levels of pain experience more physical impact of MS whereas those who report higher levels of discomfort suffer from more emotional illness intrusiveness. MS impacts differently based on report of "pain" or "discomfort", not in terms of overall impact but in direction of impact.

This study shows that people found Pain and Discomfort equally disruptive in their lives. The most interesting findings were those where the links were different. The distinction between whether sensations were reported as "pain" or "discomfort" was an important one. Those who had more "pain" had more physical symptoms, whereas those with "discomfort" had more emotional symptoms. Clinically, it is likely that emotional distress will be more of a feature in patients reporting discomfort, rather than pain, and their emotional needs must be addressed.

There are different possibilities to explain these results. One is that if people who mainly have emotional pain report it as discomfort, we would reasonably expect to find this relationship. Another is that both have the same or similar sensations but that the act of terming it pain leads to less distress. There, of course, may be many other alternatives.

There may be a labelling issue being detected. Some MS patients may have had clinicians that have labelled their symptoms as either pain or not pain. They may have read about pain in MS on the Internet, in newspaper or magazine articles. The label given by the clinician may have determined the patient's perception of this symptom. Alternatively, the adoption of the label may have been determined by the patient's perception of this symptom.

These issues highlight the importance of perception. One's physical symptoms do not directly lead to a lower HQOL; instead it is the assessment of those symptoms that may or may not lead to a reduced quality of life. If factors